

# INDIAN SCIENCE

## Transforming **INDIA**

A **Look** Back on Its **70-Year** Journey

### Impact of Science in **INDEPENDENT INDIA**

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## About the Cover

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From a newly independent country learning to govern itself to a nation with capability of developing and launching rockets, India has come a long way. Indian science and technology has had a major role in this feat. The cover page aims to capture this transformation. The photo used on the cover page shows Indian national flag hoisted at Chandni Chowk in New Delhi on August 15, 1947.

(Photo Credit: By photodivision.gov.in - <http://photodivision.gov.in/waterMarkdetails.asp?id=869.jpg>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=19526626>)

# INDIAN SCIENCE

## Transforming **INDIA**

Impact of Science in **INDEPENDENT INDIA**



**Indian National Science Academy**

Bahadur Shah Zafar Marg, New Delhi





# Preface

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While pursuit of science as a profession started only recently, it has always been a part of human cultural evolution, particularly since agriculture started 12,000 years ago. From health to space travel, science has made a major impact on society. Even though our better quality of life is due to tremendous progress in science and technology over the years, this is not always reflected in the public perception of science. The blame for this perception is placed usually on us scientists. We don't communicate well to society at large what science is, how it is practiced, how it impacts our day to day life etc. In an attempt to address this lacuna, we present here a narration of stories of the impact that scientific research carried out in post-independent India has had on our society.

When it became independent, India was poorest of the poor countries with a literacy rate of just around 12% and average life expectancy of about 32 years. At the same time, it had a very large, culturally diverse population compared to many other countries born after WWII. Today, in just 70 years, India is one of the top five economies in the world. This is not a mean feat.

What made this remarkable transformation possible was the application of Science and Technology in building the nation, which resulted in self-sufficiency in food and better healthcare for more than 1 billion people. It also gave birth to a whole generation of self-confident Indians who took up adventurous career paths in India and abroad, paving the way for the country's contribution to academics, basic science, IT, pharma industry, space research, and other sectors world-wide.

The stories presented in this book showcase some of the milestones in this journey of transformation. We have chosen those that are less known to the public and our narrative is in a story-telling style. There are no big heroes in these stories. The major players here are the ability of our society to pursue basic & applied scientific research even in difficult situations and the strengths of our science and mathematics education.

Each story narrates how science & mathematics research being carried out in educational and research institutes has provided the necessary scientific and technical capabilities required to develop, adopt, modify, and improvise technology for public good.

Way Forward: Developing the nation is a work in progress. A very large part of the population is still reeling under poverty. Social and economic inequality is extremely high in India. The current mode of development is unsustainable given diminishing natural resources due to over-exploitation and due to the impact of climate change and global warming. All nations in the world, be they developed or developing, are reorienting their education system to be future-ready to achieve sustainable development goals. Scientific temper, rationality and analytical and critical thinking are basic goals of modern education to maintain peace and harmony. Students are being trained in research and innovation skills in both basic and applied sciences. Hopefully, these efforts make the students *future-ready to solve, what today we consider, unsolvable problems in science and technology*.

To secure India's leading position in the knowledge economy of the millennium, we too need to develop innovative methods of science education. Modernising Indian science education would not only help Indian society, but it would impact the entire world given India's demography.

INSA sincerely hopes that this book will inspire more and more scientists to come forward to narrate their (or their peers') stories wherein teaching/training and research in science and mathematics have made a visible impact to the society.

**Ajay K. Sood** FRS

President, INSA

# Editor's Note

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India's journey from 1947 to today is remarkable. No society, as large as India and as diverse as India, in the known history, has transformed itself in just two human generations (~60 years). All this was possible because we relied on science and technology. We invested in educating the masses in science and technology. We expanded and strengthened our bases in the basic understanding of science and its application to solve societal problems.

Stories collated here reflect the arduous, but, exciting, journey that India went through since Independence. These are the stories scripted by our scientists and technocrats using unique solutions that are most appropriate for India, given the prevailing conditions and availability of resources.

These stories are representatives of many more such success stories, which indicate that:

1. But for good understanding of basic science amongst the teaching community, we wouldn't have been able to come this far.
2. But for the good research that we do in our universities and institutes, we wouldn't have had such a good teaching community.
3. But for general understanding and respect for science in our society, this large a number of people wouldn't have opted for science education and/or research.

I thank the authors of the stories in this book: Adita Joshi, Kavita Tiwari, Dinesh Sharma and Nissy Nevil for their efforts in collecting and collating the information and also writing the stories in a way understandable to general public. I sincerely acknowledge and appreciate inputs, comments and suggestions from Srishti Dar, Shanti Kalipatnapu, Shraddha Karve and Nivedita Subramaniam, which have greatly helped improving the narration of these stories. Thanks to Arati Halbe, Spoorthy Raman and Dennis Joy of Gubbi Labs for extensively reviewing and correcting the stories and making infographics and to Anson Advertising & Marketing for design and layout of this book. Special thanks to Shanti Kalipatnapu and Pranali Patil for their efforts at all stages to bring out this book.

I am conscious of the fact that there many players in each story, whose names may not have appeared in these stories. More importance is given to the science, to the process of identifying the problems and the ways they were solved. Nevertheless, for the purpose of narration style, efforts of certain individuals are highlighted. Any omissions of names of other players are unintentional and I sincerely seek their forgiveness.

**L.S. Shashidhara** FNA  
IISER Pune

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## The violet line of control: Indelible ink

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*By Adita Joshi*

Spring of 2017 in the Indian capital of Delhi was fading away with the summer slowly setting in. Other than the soaring temperature, the Delhi Municipal elections were adding to the heat in the city. Like most of us, I dutifully voted. Marked on my index finger nail and skin, was a violet line from a 10 ml bottle; a testimony that I voted and thereby, participated in an essential activity of the largest democracy in the world. It was a Sunday, and that 'Delhi evening' was consumed by coffee table and newsroom discussions on the fate of the elections.

My fingers were busy switching news channels when my nine year old son, Avi, reached out for the remote control. He was almost trying to snatch it away, wanting to change to something more exciting than a news channel. Not approving, I raised my finger and warned him of the consequences of his behaviour. Avi retracted, but the next moment he came near and held my hand. I expected some cajoling to calm my anger.

"What is that Momma?", he asked, pointing at the violet mark on my fingernail.

"Were you colouring?", he questioned. His curiosity to find the source of the mark could be felt.

"No honey, I wasn't colouring", I replied.

"Then what is it?", his eyes ogled onto mine, seeking a definite answer.

"It is called the voting ink. When I voted today, the poll officers put it on my nail. It is a proof of my duty as a citizen", I explained.

"Oh! You are selecting leaders", Avi smirked. I asked him how he knew that.

"I read it in my social studies book that it is the duty of everyone to vote, but I didn't know they colour your finger as well", he replied.

After a couple of days, the results of the elections were out and it was a perfect topic for a dinner conversation. While eating, Avi reacted in profound surprise,

“Hey Momma! It is still there! And now it looks black”, he quipped.

“The mark is going to stay for a few more days dear”, I said and before I completed, his surprise and suspicion knew no bounds. “What? How? Can't you wash it away with soap?”, he sent a tirade of questions.

“Soap cannot wash it away, it cannot be erased and it will go away on its own as time passes”, I told him. His questions did not stop.

“What makes the mark so stubborn? Who made this ink? Does your skin feel alright?”, he went on asking such important questions – questions that most of us may not have answers to, until we sought information on.

I felt belittled by the young boy's inquisitiveness and I started thinking. Who gave the idea of marking the voters? What human endeavour has gone into manufacturing of the violet liquid? When and where was the ink used in electoral process? A number of such questions raced through my mind. Consumed by this curiosity, I began my inquiry into reading and investigating about the origin of the 'election ink'. This time it was important to me; I felt that I owed it to Avi. Two days later, I called Avi to provide answers to some of his questions.

The 'election ink' is popularly known as the 'voter's ink' or 'indelible ink'. Indelible means 'irremovable' or 'permanent'. Dr. Salimuzzaman Siddiqui, one of the most distinguished organic chemists in the country, first developed the composition of indelible ink. It was first used, albeit on small scale at a few polling booths, in the Indian Provincial Election of 1946 to mark the thumb of voters.

## **Early phase of ink development:**

### **Pre-Independence**

The initial efforts towards developing the ink in India began in the mid 1940s. Dr. Shanti Swaroop Bhatnagar, the then Director General of the Indian Council of Scientific and Industrial Research (ICSIR) approached Dr. Siddiqui to start developing a formulation of indelible ink.

Dr. S.M. Ismail, in his writings, has quoted a narration by Dr. Siddiqui as – “Bhatnagar sent a sample containing silver chloride, which when applied, would not stain the skin until much later. I fixed it with silver bromide and the staining power improved instantly. I sent the sample back with the same messenger who had brought it. It was shown to eight members of the Election Commission, all of who tried it on their fingertips. It instantly dyed their skin.”



"I see! The scientist changed chloride to bromide and it worked? He was indeed a smart chemist, he did it so quickly", Avi remarked. I smiled, for Avi did not know the difference between a bromide salt vs. a chloride salt, but he could decipher the trick applied by the scientist.

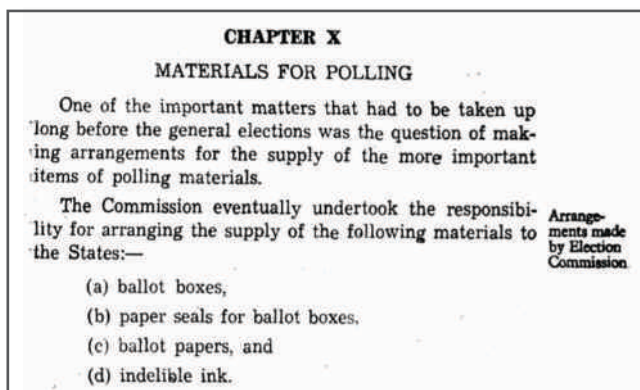


*Dr. Salimuzzaman Siddiqui did his doctoral research work at the University of Frankfurt, Germany under eminent chemist Julius von Braun. He joined Indian Council of Scientific and Industrial Research in 1940s, and later migrated to Pakistan in 1951 upon the request of Nawabzada Liaquat Ali Khan.*

*(Photo Courtesy: Hamdard Foundation)*

## Post-Independence

The next phase of ink development began soon after India's independence from the British in 1947. The first general elections were to be held in 1951-52 and were perceived no less than a grand festival. The electoral festivity, like any other merriment, required mammoth scale preparations, and also brought unforeseen challenges. The responsibility of conducting fair and smooth elections was a major task for the Election Commission of India. Sukumar Sen, the then Chief Election Commissioner, and his team, started planning in advance, and listed out indelible ink as one of the four important polling materials to be supplied to all states by the Election Commission.



*An excerpt from the "Report on the first general elections in India 1951-52". Published by the Election commission of India. Volume I (General); Page 95 (1955).*

The idea of using indelible ink was not new; the ink was previously used in other countries where it was difficult to verify identity of the voter using document-based proofs. The importance of first ever elections in a newly formed democracy can never be stressed enough. It was extremely important to ensure that everyone got to exercise their right, and no cheating or multiple voting by same person happens. Such incidences could kill the essence of Indian Democracy.

“But why would anyone vote in place of others or more than once?”, Avi asked. “Maybe to make their favourite person win!”, he answered his own question.

I was deeply motivated by the young boy's involvement with the ink story. While turning the pages of the 'Report on First General Elections in India', I discovered a text highlighting this problem and a possible solution. The excerpt reads as follows:

*“The special provision made in rule 22 of the Representation of the People (Conduct of Elections and Election Petitions) Rules, 1951, for preventing personating of electors, requires that the voter shall, before receiving his ballot paper, allow inspection of his left forefinger to the Presiding Officer or a Polling Officer. If his finger bears no mark of indelible ink, then only a ballot paper will be issued to the voter, but the finger would first be marked with indelible ink.”*

The number of voters in the first election was huge. Though the centre and state administration adopted various measures to ensure a fair election, they could not ensure that there is no cheating or multiple voting. Marking the voter for voting once was essential. At that time, such an ink was not made in India, so what could they do? There was one solution – to import the ink from Great Britain.

Importing the ink from Britain would have been an action of demonstrating India's insufficiency. This decision would have marked continued dependency on the British. India, a newly independent nation, was fierce about proving its independence and self-sufficiency, and hence, the only solution to this problem was to make the ink in India.

## **The first marks of ink development**

This huge responsibility of developing the indelible ink in India lay on the scientists from the Chemical Sciences division of the National Physical Laboratory (NPL) in Delhi. They were assigned the task of formulating the composition of such ink. NPL, at that time, was one of the first few CSIR laboratories established in Independent India. Soon after NPL was established, an 'Ink Development Unit' (IDU) was set up and it had a pilot plant and machinery to manufacture all types of ink.



*National Physical Laboratory, New Delhi: The birthplace of the indelible ink*  
(Photo Source: <http://www.csir.res.in/gallery/national-physical-laboratory-npl-new-delhi>)

Dr. Siddiqui was closely involved with the ink development unit at NPL. Postal stamping ink and printing inks were also being manufactured in the ink development unit. About 15,000 lb (or 6803 kg) of stamping ink was manufactured and supplied to posts and telegraph department in the year 1949.

Dr. M.L. Goel, a young chemist who had established the Chemical Division at NPL, took over the task of developing the formulation of the indelible ink. The team included eminent chemists like Dr. B.G. Mathur and Dr. V.D. Puri along with a group of inspired, young chemists. With a dedicated team at work, the formulation and development of the indelible ink did not take long. It was developed and manufactured at NPL during 1950-51.

India is a nation where history has witnessed many examples of odd wins and unfair losses. While the scientists gave their best composition for indelible ink, the fidelity of the ink was questioned in some time. Soon after the first elections, the indelible ink came under a scanner of criticism. There were reservations on the indelible nature of the ink. Though a check by the authorities did not find any evidence to challenge the indelible nature of the ink, the scepticism was rife.

In this backdrop, the Election Commission came up with a report on this issue before the second general elections that stated – “No demonstration has yet been given before the

Commission by anyone to justify the criticism. At an all-parties conference in 1956, the Election Commission offered the deletion of the legal provision regarding the marking of the voter's finger with indelible ink in case the political parties really felt that it was ineffective. It is significant that all the parties desired the provision to remain. The provision was accordingly allowed to remain on the Statute Book."

During the first general elections there were 93 cases in the whole of India in which the poll had to be adjourned under section 57 of the Representation of the People Act, 1951, for the following reasons :—

- (i) interchange of ballot papers;
- (ii) non-supply of the electoral roll at the polling stations;
- (iii) breach of law and order;
- (iv) loss of ballot papers;
- (v) inclement weather;
- (vi) defective ballot boxes;
- (vii) defective indelible ink;
- (viii) mistake in pasting symbols on the ballot boxes;
- (ix) failure to provide a sufficient number of ballot boxes; and
- (x) tampering of ballot boxes or paper seals during poll.

*An excerpt from the 'Report on the first general elections in India 1951-52'. Published by the Election commission of India. Volume I (General) (1955).*

The indelible ink thus maintained its position in the statute book for the second general election. However, people continued giving alternatives. One of the suggestions that arrived on the eve of the second general elections was to vaccinate or revaccinate voters for small pox before receiving any ballot paper. The argument was that a vaccination mark remains fresh and detectable for about a week and can restrict impersonation.

While the idea served the purpose of fighting small pox, its execution required favourable public opinion, agreement from political parties, laws for making revaccination compulsory, participation of public health officials for mass inoculations, and polls to be held in the season when small pox breaks out. The Election Commission, while considering this suggestion, observed the following – *"If it is ultimately decided to adopt the scheme, it may be extended in the first instance to city and industrial areas from where complaints are usually received that the same person has voted more than once after obliterating somehow the indelible ink-mark."*

However, the idea of vaccination never saw the light of the day. Indelible ink was again used as an important and mandatory polling material against fraudulent voting. Scientists at the IDU at NPL were involved in supplying 3,16,707 phials (bottles) of indelible ink for conducting the second general elections of 1957.



**The marking goes on:** (Left) A Polling Officer affixes indelible ink mark on the fore-finger of a voter before allowing her to cast the vote at a polling station in Delhi on 14 January 1952

(Photo Credit: By Photo Division, Ministry of Information & Broadcasting, Government of India - [http://www.oldindianphotos.in/2014/04/first-lok-sabha-general-election-scenes\\_15.html](http://www.oldindianphotos.in/2014/04/first-lok-sabha-general-election-scenes_15.html), Public Domain, <https://commons.wikimedia.org/w/index.php?curid=59761090>)

(Right) A finger showing the application of indelible ink from the base of nail of the index finger to the boundary of the first joint of the index finger

(Photo Courtesy: By GaneshBhakt - Own work, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=15081480>)

## The birth of the 'Mysore Ink'

Though NPL, the creator of the indelible ink, did a fascinating job for the production and supply of ink for elections, it could not sustain this operation, as it had to shift its focus on other areas. Thus arose a need for licensing the ink production to a public-private entity. After a few considerations, Mysore Paints, a small public sector paint manufacturing company from Karnataka, was chosen for ink production.

Mysore Paints, formerly known as the Mysore Lac Factory, was established in 1937 by the Maharaja of Mysore Nalwadi Krishnaraja Wodeyar. This was started to harvest lac from local forests, make sealing wax and provide employment to regional community. Mysore was one



of the prosperous princely states during the time which flourished under the rule of Krishnaraja Wodeyar prior to independence. In 1947, the company was acquired by the erstwhile Mysore State and was renamed as Mysore Lac and Paints Limited.

For the general elections of 1962, Mysore Paints supplied 3,72,923 phials of indelible ink to various states at a total cost of Rs. 2,94,607. Thus the now famous 'Mysore Ink' was born. In 1989, the company was renamed as Mysore Paints and Varnish Limited (MPVL). Today, the company receives purchase orders from the office of the Chief Electoral Officer of individual states during elections. Apart from the indelible ink, the company's first product, sealing wax, is still used during elections for securing ballot boxes. Today, the indelible 'Mysore Ink' is exported to about 25 countries.

### The Globetrotter

Towards export, MPVL got its first order for exporting indelible ink to Ghana and then exported it to Singapore in 1978. MPVL exports the ink to more than 15 countries. A few of them are neighboring countries such as Nepal, Malaysia, Maldives and other countries including Ghana, Mongolia, Canada, South Africa, Turkey and Nigeria. MPVL caters to various specifications as per the countries and customers demand.



A few countries require voters to dip their fingers into the ink. In some places brush is used for application, whereas other countries use a nozzle applicator. Indelible ink marker pens are also used in a few countries and Election Commission of India is also considering using these marker pens in future.

As per MPVL annual report 2015-16, indelible ink contributed to 80.95% of the total turnover of the company and accounted for about Rs. 30,92,26,711.00 as value of sales.

"Oh! That means people of all these countries wear India's ink after they vote. This is really awesome", remarked Avi, who was keenly listening to this story, with inexplicable pride.

Soon, the Ministry of Law & Justice, Government of India, through the Election Commission of India (ECI) contacted MPVL and after several meetings, it was agreed that MPVL would produce and supply the ink for all elections henceforth. The formula of the indelible ink was patented by National Research Development Council (NRDC), thus prohibiting other companies from

manufacturing the ink. Since then, MPVL has been the sole supplier of indelible ink across the country and beyond, and enjoys more than 50 years of trust with the government.

## The chemistry of the Indelible Ink

So, what is the ink, that we are so proud of wearing, actually made up of? The ink contains silver nitrate, which reacts with our skin in the presence of light, to impart the colour. The mark fades away once the skin and nail cells are replaced, in about 2-4 weeks. The concentration of silver nitrate varies from 10%-25%. The ink also contains certain dyes. Since the ink is sensitive to light, it is stored in amber coloured plastic bottles. The formulation is water based and contains alcohol, which facilitates faster drying after the ink is applied.

The original formulation of the ink had not changed for a long time since 1962. In 2001, Dr. Krishan Lal, the then Director of NPL, proposed to develop a better formulation of ink that could dry faster than the original formulation. The need of a new formulation arose, as there were a few reports that the ink mark could be removed within 40 seconds of its application, before it dried. Now, scientists were looking at removing the water base from the ink to make it dry faster. That time, the Election Commission was targeting the 2004 Assam state elections, and wanted to use the new formula. The proposal was discussed with the Election Commission, NRDC and MPVL.

“Each element, compound or a molecule has individuality, a specific nature. The beauty of chemistry is that when a few compounds or elements come together, the outcome is a new property. While these properties can be mostly predicted, sometimes we face unexpected outcomes”, remarks Mr. Niranjan Singh, Principal Technical Officer at NPL, who was involved in the advancement of indelible ink.

The new idea was funded by the Election Commission during 2001-2002 with a total amount of Rs.5.290 lakhs given to NPL for research. The team, involving Dr. A.K. Sarkar, Dr. Prabhat Gupta and Mr. Singh, worked on advancing the drying properties of the ink. The scientists formulated a composition without a water base that could dry faster than the previous version and the colour would last longer. But there were challenges.

“The colour of the new ink formulation came out to be saffron. The Election Commission had reservations about using the colour saffron as it is endorsed by a few political groups”, says Dr. Krishan Lal. Another attempt to make the ink dry faster resulted in a two-step process involving application of a sensitizer followed by application of the ink without a water base. In principle, the concept worked. However, the Election Commission officials found the method of application too cumbersome to be adopted.

The team at NPL made another formulation that was quick to dry and was totally resistant to manipulation, but it was pinkish red in colour. The Election Commission had to reject this formulation too as the colour resembled 'alta' or Rose Bengal – a dye commonly applied by women in the states of Assam, Bengal, Bihar, Odisha and Eastern UP.

Today, though NPL has handed over the production and distribution of indelible ink to MPVL, it still plays a pivotal role. Till date, before the commencement of any election, the Election Commission sends a 10 ml vial from MPVL to NPL for quality testing. The ink is tested specially for the concentration of silver nitrate – the main chemical that defines the staining of the ink. The scientist/staff at NPL check it for composition as well as concentration of individual components. It is only after the test that large-scale manufacturing begins at MPVL. NPL still receives the royalty for the ink.

## **Demonetization – A race against time**

On November 8, 2016, Prime Minister Narendra Modi announced demonetisation of Rs. 500 and Rs. 1000 currency notes to counter black money. While the nation scrambled to return/exchange the banned notes, and queued in front of banks and ATMs, the employees at MPVL had a different challenge to address. Their perseverance and struggle to keep up their commitment was put to test during the recent demonetization exercise.

But what did MPVL have to do with demonetization, you wonder? As a part of the demonetization exercise, the government allowed people to exchange the banned notes for new currency notes of Rs. 500 and Rs. 2000. The banks allowed a maximum of Rs. 4500 to be exchanged in a single day. But how would the bank keep track of the number of visits one person was making to the banks in a day? That is where the indelible ink played a huge role. The government, together with the Reserve Bank of India, decided to use the indelible ink to ensure that a single person exchanges money only once. The strategy was to mark each person before exchanging the notes.

To address the need for ink, the government asked MPVL to produce about 2.9 lakhs of 5 ml bottles of the indelible ink. For MPVL it was an urgent, huge, and unexpected order, but more so a desperate national situation. The staff and workers of MPVL worked for extra hours and initially 30,000 bottles were dispatched within a few days. Each bottle was priced at Rs.116 and could be used to mark about 500 people.

Branches of State Bank of India (SBI), Bank of India, Canara Bank and the RBI's Delhi office adopted the use of indelible ink within a week of the announcement of the currency ban. MPVL successfully produced approximately 35,000 bottles of ink per day, to meet the



nationwide requirements. The finance ministry had instructed Bharatiya Reserve Bank Note Mudran Private Limited (BRBNMPL) to distribute the ink to various banks and RBI regional centres. The indelible ink packages were airlifted to various corners of the country to curb multiple exchanges by black money hoarders.



*Indelible Ink Production: Indelible ink assembly line at Mysore Paints and Varnish Limited (left)  
(Photo Source: Hindu images)*

*A package of single vial for use in India (Top right), and use in Malaysia (Bottom right) - another country which imports the ink from India.*

*(Photo Courtesy: Mysore Paints)*

## A mark of our democracy

Today, it is a constitutional requirement to mark the left forefinger of a voter with indelible ink. But, did you know that there have been changes to where the mark is put? Historically, the mark was made as a dot on the base of the forefinger. By 1962, the application changed and the mark was put just above the root of nail on the skin. Since 2006, the mark is made bigger and now the ink is applied using a brush from the top end of the nail to the bottom of the first joint of the index finger. This measure was taken by the Election commission to make sure there is no improper application of the ink.

While the scientists who devised the formula of the indelible ink are long gone, they have left a mark of their contribution, quite literally. For a country that is the largest democracy in the world, every election is a proud moment. And the violet streak of the indelible ink is

synonymous to our right and our duty to vote. The innumerable contributions of each of the scientists at NPL and the workers of MPVL have transformed India from a country dependent on import of election ink to one that exports ink to about 25 countries!

The indelible ink's odyssey of almost seven decades has demonstrated effectiveness and popularity; it has stood the test of time and so far, no better alternative has ever been successful in replacing it. The violet line marks an eternal combat against electoral malpractices, and is the guard of our democracy. As much as we are proud of our democracy, we may well be proud of the humble ink that is a mark of democracy. It is also mark of the quality of the work of our scientists.

## Acknowledgements

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# FACTS ABOUT INDELIBLE INK

1 The ink comes in vials of 5 ml, 7.5 ml, 10 ml, 20 ml, 60 ml, 80 ml and 100 ml.



2 National Research Development Council (NRDC) holds patent for Indelible Ink. It is licenced to Mysore Paints and Varnish Limited (MPVL), renewed every 5 years. NRDC receives royalty on the total amount of sales, annually.



3 National Physical Laboratory (NPL) is the testing agency of indelible ink, for which it is entitled to levy test charges.



4 Election Commission of India (ECI) is the client of indelible ink.



5 Ghana was the first country to import the ink from MPVL.



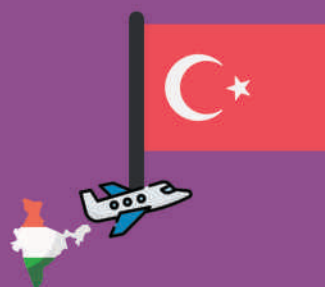
6 The composition of ink varies according to what country it will be used in. Each country requires indelible ink according to its own specification.



7 MPVL supplies versions of ink where different dye components are used. To address a market demand, MPVL also manufactures versions of ink where silver nitrate is not used.



8 Turkey is the largest importer of the indelible ink from India.





## Information Technology: How a revolution was seeded

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*By Dinesh Sharma*

India has made tremendous progress in information technology and is today considered a leading global player in the technology outsourcing business. Not just this, the use of information technology within the country is growing fast. We are truly entering the so-called information or digital age. The use of digital technologies in delivery of services useful to citizens is a noteworthy development and this has benefited, directly or indirectly, more than a billion people in the country.

While it is true that much of this growth of digital technologies in the twenty first century is fuelled by the spread of the Internet and mobile telephony, it would be wrong to presume that the fruits of information and communication technologies were not reaching the people earlier. In fact, India pioneered e-governance much ahead of others globally, and even before the term was coined. The tale of information technology in India spans 70 years, and it is interwoven with the development of science and technology in independent India.

The story of computers began unfolding in the 1930s and 1940s under the guidance of two leaders of Indian science in the mid-twentieth century—physicist-turned-statistician Prasanta Chandra Mahalanobis in Calcutta, and physicist Homi Jehangir Bhabha in Bombay. Both felt the need for computing machines while pursuing their respective scientific projects. They believed in making India self-reliant in every field of activity and also using science and technology for industrial development and economic growth. Given their key role in policy making, both Bhabha and Mahalanobis helped shape policies for electronics and computer industries in the first two decades after independence. It is a result of those early steps that India can claim to be an IT powerhouse today.

### Early analogue computers

Mahalanobis was among the earliest to have used a tabulating machine and one of the first to recognize the importance of such machines for scientific work (1). He had installed a mechanical tabulator at his own expense at his home in 1921 to help him in his statistical

calculations. In April 1932, he founded the Indian Statistical Institute (ISI) as a non-profit society, which introduced the use of mechanical desk calculators for the first time in India. Over the next two decades, ISI played a major role in introducing mechanical, electrical and electronic computing machines in India. Since import of equipment was difficult after the Second World War, Mahalanobis set up a facility in September 1943 to develop and fabricate computing machines locally. It was named Indian Calculating Machine and Scientific Instrument Research Society.

### Analogue vs. Digital computers

Analogue computers use continuously varying signals like temperature, pressure, voltages, etc., to model a mathematical problem. Control engineers do the job of converting a mechanical system to its electrical analogy, and make a mathematical model for computation. After the modeling has been done, the computation becomes very easy and convenient.

Digital computers, on the other hand, deal with mathematical variables in form of numbers that represent discrete values of physical quantities. Here each variable is converted into numbers and each number into its binary form, a combination of which does the calculation. All modern day computers, laptops and phones are digital computers.

Two new recruits at ISI, Samarendra Kumar Mitra and Soumyendra Mohan Bose, were tasked by Mahalanobis to design and fabricate an analogue computer. They developed India's first 'analogue electronic computer' in 1953, mostly using recycled components with some parts fabricated at the institute's workshops. Mitra published a scientific paper on this feat in the *Review of Scientific Instruments* in May 1955 (2). Subsequently, ISI acquired Hollerith Electronic Computer (HEC-2M) in February 1956 from British Tabulating Machines (BTM). It was used to solve scientific problems in academia from different institutes - Indian Association for the Cultivation of Science in Calcutta, the Indian Institute of Science in Bangalore, IIT Kharagpur, the Tata Institute of Fundamental Research (TIFR) in Bombay and the Physical Research Laboratory in Ahmedabad (3).

Making full use of his international networks, Mahalanobis got another large electronic computer - Ural from the USSR. With two large, modern computers in tow by 1959, ISI virtually became the national computer centre. Several research bodies such as the Atomic Energy Establishment (AEE), defence research laboratories, and leading universities like Banaras Hindu University (BHU) were using the two computers to solve their scientific problems. Both HEC and Ural were first generation machines.

The idea of developing a second-generation digital computer system took shape when Jadavapur University approached ISI to work on such a system jointly. In 1961, the two institutes came together to design a new project for the development of second generation, transistor-based computer. The result of this collaboration was a prototype of a new computer – ISIJU-1.

In Bombay, Bhabha led the efforts in early computer development at TIFR – an institute founded by him in 1945. One of the areas of research he initiated was particle research using balloons, for which he needed help in instrumentation. The balloons that were to be flown to high altitudes carried battery-operated instruments called Geiger-Muller counters, to measure the total intensity and vertical component of cosmic rays. For helping him in instrumentation, Bhabha recruited A.S. Rao, an electrical engineering graduate from Stanford University. Subsequent to his participation in balloon experiments, Rao set up an Electronics Production Unit at TIFR in 1952 and then moved over to AEE along with Dr. Raja Ramanna, to work on instrumentation for *Apsara*, the first nuclear reactor.

When the Department of Atomic Energy (DAE) was established in 1954, Rao started planning for further work in nuclear electronics. In 1959, the electronics group developed an analogue computer capable of solving large mathematical problems involved in designing control systems for nuclear reactors. In 1963, the team came up with a 15-amplifier version of a self-contained general-purpose analogue computer, EAC-62. Later, the group designed a transistorized, high performance analogue computer. It was this group that was later hived off into an independent public sector production unit called the Electronics Corporation of India Limited (ECIL).

Another analogue computer was designed and fabricated at the Indian Institute of Science in Bangalore during 1954-56. Its inventor was Vincent C. Rideout (1914-2003), who had come to the institute as a visiting Professor from the University of Wisconsin, Madison, USA. Rideout had brought with him several components and sub-assemblies, including operational amplifiers required for fabrication of the analogue computer (4). Members of the faculty and students of the Department of Electrical Communication Engineering participated in this exercise. The computer was named Philbrick-Rideout Electronic Differential Analyzer, PREDA for short. One of the student volunteers in this project was a fresh engineering graduate, Vaidyeswaran Rajaraman.

The three Indian computer systems discussed so far – Samrendra Mitra's machine at ISI, Rao's machine at Trombay and PREDA developed in Bangalore – were all analogue computers or special purpose machines designed for specific applications only.



## The 5 generations of computers

**First Generation – Vacuum Tubes (1940 – 1956)** – The first computers used huge vacuum tubes as circuitry and magnetic drums for memory. They were as big as a room and cost a fortune, in addition to generating a lot of heat and being energy hungry. They worked using machine language – 0s and 1s. Punched cards were used for data input and the output was through printouts.

**Second Generation – Transistors (1956 – 1963)** – Transistors, invented in the 1940s, gradually replaced vacuum tubes in the next generation of computers. This made computers smaller, faster, cheaper and less energy consuming. The programming language evolved from cryptic binary to 'assembly' languages. These machines stored the instructions in their memories

**Third Generation – Integrated Circuits (1964 – 1971)** – Transistors were now being miniaturised and put on silicon chips, leading to increased speed and efficiency. These machines used keyboards and monitors for input/output and an operating system for interface. This ease of use resulted in a new mass market of users.

**Fourth Generation – Microprocessors (1972 – 2010)** – Powered by the 'Intel' technology of microprocessors, which positioned all computer components onto a single chip, the size of a computer reduced drastically. Microprocessor based computers quickly became common for home use and companies like IBM and Apple launched 'desktops'. Microprocessors even moved beyond the realm of computers and into an increasing number of everyday products.

**Fifth Generation – Artificial Intelligence (2010 – )** – The present generation of computers are based on artificial intelligence – the ability to 'think' and 'respond' based on the context with machines that can process and respond to natural language, and have capability to learn and organise themselves. The future looks to be transformed with technologies like quantum computation, molecular and nano technology.

## India's first digital computer

Bhabha was keen to see scientists develop a modern computer that could help design and run nuclear reactors. Bhabha tasked R. Narasimhan, a graduate in electrical engineering and a doctorate in mathematics from the Indiana University, USA, with the development of a digital computer that was to be a 'full scale, general purpose, and digital computer using contemporary technology'. Except Narasimhan, no one in the six-member team had ever

used or operated a computer (5). The project was executed in two steps– the first involved the design and construction of a pilot machine to serve as a proving ground for ideas in circuit and logic system design. Based on this experience, work on a full-scale machine was started in 1957 and it was fabricated by 1959. The imported components used in fabricating the machine included control unit, arithmetic unit, drivers, memory units and core stacks, input console (tape recorder), teleprinters, magnetic tape storage (including tape drive) and part of power supplies. The value of all these sub-systems and components was Rs. 263,651 (6) and the total cost, including imported components, was Rs. 800,000.

The hardware in the central processor consisted of 2700 vacuum tubes, 1700 Germanium diodes and 12,500 resistors. The computer deployed Ferrite core memory with a capacity of 2048 words and memory cycle of 15 microseconds. Its memory cycle time, as well as 40 bit word length, were both higher than the first generation IBM machine, IBM 701. This computer took 45 microseconds for addition and subtraction, while multiplication and division took 500 microseconds. The machine, christened TIFR Automatic Calculator (TIFRAC) was commissioned for routine work in the third week of February 1960.

Similar machines built by universities and atomic energy groups in the U.S. had influenced the design philosophy of the TIFR computer. The design of this computer in 1957 was still not very much behind what was being attempted elsewhere in the world. But by the time it was commissioned in early 1960, technology had progressed much faster, making it already obsolete. In the words of Narasimhan, “The pilot machine, except for its size, was quite in pace with the state of the art in 1954. The design of TIFRAC in 1957 was still not very much behind what was being attempted at that time elsewhere. But by the time, it was commissioned in 1960, computer technology had surged ahead leaving our machine behind as an obsolete first generation machine (7).”

Though it was not a technological breakthrough, TIFRAC was an important landmark as it helped Indian scientists gain capability in various fields of computer design, fabrication, testing, operation, maintenance and programming. A core group of specialists had grown to maturity who could tackle logical, circuit, system and engineering design of a variety of digital equipment with confidence (8). Besides scientists from AEE, the crystallography group of Madras University and TIFR used TIFRAC for data analysis. The data of early extensive air shower experiments of the cosmic ray group at TIFR was analysed using this computer (9). The project helped spread computer consciousness among research scientists beyond TIFR. By 1964, the machine operated in two shifts as scientists from government laboratories, educational institutes and private organizations from all over India used it for their computational needs.



A significant contribution of this project was the development of initial software programming capabilities. Several staff members were recruited and trained in programming. The availability of a functioning computer made it possible to recruit and train additional staff for programming (10). A programming manual was developed and an extensive library of sub-routines was set up to help users of this computer write their own programmes. Since the main and auxiliary storages of the machine were inadequate for development of compilers of any sort, programming was restricted to machine language (11). In what can be seen as a first formal effort in software programming in India, all scientists wanting to use the TIFR computer were asked to write their own programmes for solving their scientific problems.

As a report on computer activity at the institute in 1972 noted, "it would not be far wrong to say that many of the current computer users in India, handling highly sophisticated and advanced computational techniques, had their first introduction to programming through the use of TIFRAC (12)." Rocket scientist A.P.J. Abdul Kalam, later to be India's President, was among the early users of this computer. Before going to NASA's Wallops Rocket Station at Maryland, USA, for a six-month training programme in rocket science, Kalam was posted at AEE. "The first assignment given to me was to work with the TIFRAC computer team. TIFRAC was, at that time, under development and certain capabilities were in operation," Abdul Kalam recalled at a conference on computing hosted by the institute in February 2006 (13).

The CDC computer acquired by TIFR in October 1964 became a national computing facility open to academic and research community. Computer time, programming help as well as stationery were provided free in the first year. As in the case of TIFRAC, it was mandatory for all users to write and debug their own programmes. A number of programming courses were organized to help them do this, as well as to disseminate programming know-how in general.

Nearly two-dozen training courses (in 3600 Fortran, advanced 3600 Fortran, COBOL, COMPAS and SCOPE) were conducted at the TIFR, Indian Institute of Technology Bombay, University of Madras, Bhabha Atomic Research Centre (new name for AEE after Bhabha's death) and its training school, and Tata Electric Company. Individual researchers were allowed to spend time at TIFR to develop and test their own programmes. An extensive library of sub-routines was maintained and updated regularly. The programming staff developed several packages and utility programmes, while a few standard software packages were tested and made available to users.

In the first five years of its operation, over 150 institutions from all over the country used the CDC system. They included different organizations under DAE, IITs, engineering colleges, universities, science colleges, national laboratories, government and quasi-government bodies like the Reserve Bank of India and the Income Tax department, and a large number of

private sector businesses and corporations (14). Business users accounted for almost half the total number of users. These included Air India, BEST, Hindustan Lever, Godrej Soaps, Larsen and Toubro, Sandoz, Oil India, Voltas, Tata Chemicals, Tata Engineering and a number of textile and engineering firms. Several of these industrial and business organizations used the CDC computer to develop operations research programmes of their own (15).

The TIFR Computer Division decided to promote the development of large-scale applications on the CDC Computer. N Seshagiri led a team that developed Operations Research algorithms and software to optimize bus scheduling for Brihan Mumbai Electric Supply and Transport Undertaking (BEST) (16). A computer-based method for deciding optimum proportion of milk products for Aarey Milk Scheme was also developed, keeping in view the requirements of whole milk, variation in quality and constraints imposed by limitations of machinery, equipment, manpower and transport. In 1969, Seshagiri used the computer to assist in the design of satellite launch vehicles. He developed a software package called 'SIMSPACE' based on differential and algebraic simultaneous equations in numerous variables. In 1971, he developed a new concept of self-diagnosable digital systems and was one of the earliest to point out the advantages of on-board computers on satellites (17).

TIFRAC and ISIJU were taken up as research projects and commercialization was not their goal, but they helped the country develop computer consciousness among research community and also in developing capabilities in logical circuit designing and engineering design for a variety of digital system. People could be trained in programming and software using the system at TIFR. ISIJU also helped in generating a group of students and faculty in various aspects of computer technology. It was used in teaching circuit design and programming to graduate students as well as in handling research problems of a moderate size (18).

While research centres like TIFR and ISI hosted large computers for research and academic problems, these systems were also used to train a large number of people including commercial users in the initial years. Formal teaching of computer science and engineering was taken up at Indian Institutes of Technology. These institutions played a pioneering role in development of computer science education in India, thus setting a solid base for human resources development, which was a critical building block for India to emerge as a major player in the global technology business in decades to come.

The trigger for this was at IIT Kanpur where the Kanpur Indio-American Program (KIAP) was initiated. Under this, the institute acquired India's first IBM 1620 computer in 1963 and IBM 7044 in 1966. These two computers formed the core of the Computer Centre at the institute, which became the training ground for the first generation of Indian computer programmers and computer science graduates. The centre benefited not just undergraduates, graduates

and faculty of the institute, but scores of people from research, academia and industry all over the country. Harry D. Huskey (University of California, Berkley) – who was one of the three American professors who helped set up the Computer Centre - was also behind the formation of the All India Computer Users Group, which subsequently became the Computer Society of India.

Till the formal teaching of computer science began, the computers at IITK were used to run short-term, intensive courses in basics of computers and programming for academicians, industry managers and researchers interested from anywhere in the country. IBM 1620 - the core of the Computer Centre - had a central processor with core storage of 40,000 digit, three magnetic tape units and a card input-output unit. It was operational almost 24 hours a day and seven days a week. Several thousand people benefited from the short term courses. They included lectures on numerical analysis, computer logic and three hours a day of actual use of 1620.

Some 66 universities, engineering colleges, research institutes, IITs, government bodies and large industrial houses such as Tatas and DCM were represented in these short intensive courses. V. Rajaraman, who had participated in building the analogue computer at the Indian Institute of Science at Bangalore in 1950s and joined IITK in 1963, was a student in one of the first intensive courses. Biswajit Nag, Professor of Computer Science at the Jadhavpur University, who later became Secretary of DoE and Director of IIT Bombay, also took this course early on.

When intensive courses started, professors realized that they did not have any textbooks or course material to be given to the participants. So, Rajaraman started writing textbooks. The first book he wrote in 1968 was for undergraduates – on Fortran programming, numerical techniques and digital logic. The book - *Principles of Computer Programming* – sold 3000 copies in the first year. It had three editions and 14 print runs till 1992. The second one – *Computer Programming in Fortran 77* – created a record by undergoing 40 print runs till August 2003. Yet another title, *Computer Oriented Numerical Methods*, had 30 print orders from 1971 to June 2002. *Fundamentals of Computers*, first published in 1985, has been printed 27 times till October 2002(19). These books have remained a must-read for several generations of Indian programmers and computer scientists. Over the past three decades, these books have made Rajaraman a legend in this field.

In 1965, an optional course in computer science was introduced in M. Tech. Once the postgraduate course in computer science was running successfully, it was proposed that this programme should have its own admission process and be run independent of DEE. The first full-fledged M Tech course in computer science was started in 1971. Ten students from other

IITs and the Indian Institute of Science, Bangalore were admitted in the first batch. A Ph.D. programme in computer science was also initiated. In 1979, the first undergraduate degree course in computer science in India began at IIT Kanpur.

## **Policymaking and technology development**

Along with pioneering use of computers – both self-designed and fabricated as well as imported commercial machines – for research and academic purposes, the scientific leadership was also involved in shaping national policies for industrial production of electronics and computer equipment. The shortage of certain critical electronics components during the Indo-China war in 1962 led to the thinking in the government that India needed to develop indigenous capacity in electronics. During the war, Indian forces experienced shortage of electronic components like switches used in imported radars. When it was difficult to get one particular Trans-Receive switch, an urgent request was sent to TIFR and the microwave engineering group at the institute delivered these switches to the armed forces (20). It was difficult to procure strategic electronics in open markets. After the war, at the suggestion of cabinet secretary, S.S. Khera, who was a member of the Atomic Energy Commission (AEC), a committee was set up to review requirement of a range of electronic instruments including computers.

The Electronics Committee under the chairmanship of Bhabha had three members - Vikram Ambalal Sarabhai, Director of Physical Research Laboratory, Ahmedabad; Ayyagari Sambasiva Rao, Director of Electronics Group at AEE and S. Bhagvantham, Scientific Advisor to Defence Minister. Several technical experts were involved in working groups, which gave recommendations on a range of subjects. The committee was asked to recommend steps for “planned development of electronics, so that the country as a whole may become self-sufficient in this field in the shortest possible time”. The resolution setting up the committee said “electronics is the nervous system of modern technology and has assumed an important role in monitoring and control of the production process in engineering, chemical and metallurgical industries. It is vital for atomic energy, communication and defence (21).”

The committee's report, submitted to the government in 1966 after Bhabha's death, was a blueprint for development of an indigenous electronics industry based on research and development, design, training and select foreign inputs. It was a ten-year plan (1967-1975) with projections on electronics equipment and components that would be needed in different segments of the electronics industry – radio receivers, wireless radio equipment, transmitters, navigational aids, microwave systems, transistors and semiconductors, components, raw material, and electronic computers. It was observed that the design and production of

analogue computers and special purpose digital computers such as the one built by TIFR and AEE could be undertaken on the basis of expertise existing in the country. For large high-speed computer systems, it said, India would have to depend on imports or make them with foreign collaboration. Most notably, the Bhabha Committee foresaw that computers would be needed for applications in academic research, industry and engineering, planning, weather prediction, space and defence research, inventory and retrieval (census, patents, insurance, library and hospital automation), traffic and scheduling (railways, airports, hotels, ports etc.) and commercial (cost accounting, wage bills, purchase and banks) (22).

When these recommendations were made, the size of the electronics production in India was only 0.15 of the Gross National Product compared to 3.5% in Japan, which was the leader in this field. The report observed that if all the recommendations were implemented with adequate investment, it could lead to creation of up to 4 lakh new jobs by 1975, a bulk of them for engineers and scientists. The committee advocated that India should avoid 'step by step' development of electronics industry as seen in developed countries but it should leapfrog. The government accepted all recommendations of the panel, and appointed in June 1966 another Electronics Committee under the chairmanship Vikram Sarabhai to advise the government in implementation of the Bhabha Committee recommendations.

One of the first actions that followed was the establishment of the Electronics Corporation of India Limited (ECIL) in Hyderabad in April 1967, as a public sector undertaking of the DAE. The electronics production unit of AEE established by A.S. Rao was hived off as a full-fledged manufacturing company to meet the needs of not only BARC and DAE, but several other users. The first breakthrough, following the submission of the report came in the form of commercialization of Trombay Digital Computer (TDC), which was unveiled in January 1969. The technology of first of the TDC series of computers - TDC-12 – developed at BARC was transferred to ECIL for manufacturing. It hit the market in 1971. This was the first India-developed computer to have deployed semiconductor devices and made use of standard components. Dr. S. Srikantan, who developed the machine, was made head of the computer division at ECIL. This group subsequently developed a range of products - TDC-12, TDC-312, TCD-16 and TCD-332. The application products included systems for businesses, real-time process control and scientific applications. ECIL also developed India's first microcomputer, Micro 78, in 1978.

Another initiative was taken up by TIFR in 1970 in the form of the National Conference on Electronics to review the status of electronics industry since the Bhabha committee report was submitted. It discussed several scientific and other issues including licensing, foreign collaborations and indigenous research, design and development activities. The conference pointed to the need for setting up a separate administrative body in the government to

preside over all aspects of electronics development. This resulted in establishment of the Department of Electronics (DoE) and the Electronics Commission (EC). DoE was set up within the Ministry of Defence with effect from June 26, 1970. EC was constituted in February 1971. Mambillikalathil Govind Kumar Menon, Bhabha's successor at TIFR, was made the secretary of DoE.

The new department was mandated to make India self-reliant in electronics including computer technology, while EC was to 'make a comprehensive assessment, in both technical and financial terms, of national needs in for all electronic products, and integrate such needs into a single overall framework (23).' Prof. Menon established a think tank in EC called Information, Planning and Analysis Group (IPAG) to assist the commission in policy making with technical and market research reports. This was led by N. Seshagiri, who later became the Director General of National Informatics Centre. Within a short period of four years, this group produced 150 reports on various facets of the electronics industry. These reports were meant to be used as market survey documents by entrepreneurs and industrialists interested in electronics production. One such report on microcomputers inspired launch of a startup, Microcomp, in 1975. This company later became Hindustan Computers Limited (HCL).

A large number of institutions under different ministries, IITs, universities and the Indian Institute of Science participated in important R & D projects initiated and funded by DoE. One such was the Command and Control Project, under which a computer-based air defence system was developed for the Indian Air Force (IAF). The system was integrated with the existing radar system of IAF and put to operational use. It was tailor-made for ground conditions in forward areas and IAF duty pilots were involved in its development. TIFR, ECIL, the Electronics and Radar Development Establishment, Bangalore, and the Tata Electric Companies participated in this project. For the army, DoE funded development of a complete communication network from field levels to the headquarters. It involved design and development of an electronic switching system for both static and wireless applications, networking technologies and associated hardware and software.

Overall, DoE gave a large number of R & D grants in space, atomic energy and defence sectors to research institutes and PSUs like ECIL, CMC, ITI, BHEL and so on. A number of projects were conceived and executed, leading to development of skills and capabilities in those respective areas.

## **Software development and networking**

A number of initiatives were taken to develop skills in software applications. DoE founded two important national institutions– the National Informatics Centre (NIC) to provide informatics

and computer applications needs of central government departments and state governments; and the National Centre for Software Development and Computing Techniques (later renamed as National Centre for Software Technology) to develop software techniques and train software technologists. These two bodies would play a key role in shaping India's progress in information technology over the next two decades. State governments were encouraged to establish electronics development corporations, which led to start of electronics industry in many states. The electronics city in Bangalore, promoted by the Karnataka State Electronics Development Corporation later became a hub for software development. Television brands of several electronics corporations became highly popular.

Some of the national projects were executed with assistance from the United Nations Development Programme. The agency provided financial and technical assistance for a number of IT related projects including the Education and Research in Computer Networking (ERNET), Knowledge-based Computer Systems programme, and projects on computer-assisted design and computer-assisted management. The objective of these programmes was to develop expertise in application software and tools.

Besides hardware and design, ECIL played a key role in software development tools. It developed assemblers, cross assemblers compilers for languages like Fortran, COBOL and BASIC, simulators operating systems to run on TDC series of machines. In addition, it leveraged expertise available at various R&D organizations like TIFR, IITs, IIMs. For instance, N.R. Narayana Murthy, who was then working at IIM Ahmedabad, developed the BASIC compiler of ECIL. In the same way, private industry benefited from skills developed at ECIL. The entire initial team of engineers of Wipro was recruited from ECIL. The PSU also developed a number of applications related to defence, police, telecom, power sector and civil aviation.

The Computer Maintenance Corporation (CMC), established by DoE in 1975 for maintenance of IBM mainframes, soon became a leading software company. It handled major turnkey projects in domestic as well as international markets. It developed capabilities in systems analysis, design, development, implementation and support of large online systems. This resulted in execution of large computerization projects like railways freight operations, passenger reservation, banking computerization, stock exchange online systems, enterprise resource planning for large companies and bulk management of containers at ports. CMC handled projects such as electric power transmission and distribution, canal water management, gas pipeline management and process control in steel industry. It also developed capabilities in image processing techniques, resulting in fingerprint/person identification system, office automation, map digitization etc. The computerized passenger reservation system, developed by CMC for the Indian Railways, was a landmark project, which



brought the fruits of computer technology to people. It was a unique e-governance project ahead of its times. It paved the way for several large-scale computerization projects including in banks. With over million transactions every day, the system is still one of the largest such societal applications of information technology.

## Conclusion

Computer development activity in India began as part of research projects of leading scientists soon after independence. Indigenous systems were fabricated and research and academic institutions imported modern machines. However, the use of such systems was opened up to a large number of users including private industry. These computers were used as a national resource and put to optimum use. This led to not just computer literacy within and outside government users, but facilitated development of a large pool of manpower trained in computer programming. In the next phase of development, design and manufacturing activity began in public sector units, mainly ECIL. Though it may not have been a commercial success, ECIL gave birth to another set of engineers and programmers versatile in hardware and software. In the same way, CMC was the cradle of maintenance and software engineers exposed to a range of computer systems. NCSDCT worked in cutting edge areas of software development. On the other hand, IITs trained a large number of people on latest computers. All these activities in the 1960s and 1970s resulted in a pool of highly skilled people. These skills and knowledge became available to private sector industry – first hardware and then software – which took birth in the late 1970s and early 1980s with changing policy environment. A combination of these factors helped India develop skills in design, engineering, maintenance and software applications, which became useful in shaping an indigenous industry which is worth about 150 billion USD in 2017.

It is obvious that none of the early players in the field knew that IT industry would grow to this extent and would impact the country in all its economic and social spheres. That is how science contributes. Research and Education in S&T would essentially contribute to capacity building in a society to think differently, innovatively and creatively. The 1970s was a decade of green revolution, 1980s was of white revolution and 1990s was a decade of IT revolution. These collectively have made India, within 60 years or within two human generations, a confident sovereign country. The success of India is largely due to its S&T community working in colleges, universities, institutes and R&D centres across the country.

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Note: This review is based on research conducted by the author and draws from his two books – *The Long Revolution: The Birth and Growth of India's IT Industry* (HarperCollins Publishers India, 2009) and *The Outsourcer: The Story of India's IT Revolution* (MIT Press, 2015) as well as his other papers. The author is Managing Editor, India Science Wire, New Delhi.



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# The Events That Seeded INDIA'S IT REVOLUTION



**1932**

Prasanta Chandra Mahalanobis founded the Indian Statistical Institute (ISI)

**1945**

Homi Jehangir Bhabha founded the Tata Institute of Fundamental Research (TIFR)



**1953**

Samarendra Kumar Mitra & Soumyendra Mohan Bose developed India's first analogue electronic computer



**1959**

AEE developed an analogue computer capable of solving large mathematical problems involved in designing control systems for nuclear reactors

**1961**

Jadavapur University and ISI developed ISIJU, a transistor based second generation computer



**1967**

The Electronics Corporation of India Limited (ECIL) was established in Hyderabad

**1975**

India's first computer manufacturing startup, Microcomp was established. Later it came to be known as Hindustan Computers Limited (HCL)

**1943**

P C Mahalanobis set up Indian Calculating Machine and Scientific Instrument Research Society to develop and fabricate computing machines locally

**1952**

A S Rao set up the Electronics Production Unit at TIFR



**1956**

PREDAC, an analogue computer was designed and fabricated at the Indian Institute of Science, Bangalore

**1960**

TIFR Automatic Calculator (TIFRAC), India's first digital computer, was commissioned for work



**1963**

IIT Kanpur acquired India's first IBM 1620 computer



**1971**

Trombay Digital Computer (TDC), India's first indigenously developed computer, hit the markets. IIT Kanpur started the first full-fledged M Tech course in Computer Science





## Generic drugs – Saving lives with generosity

*By Nissy Nevil*

Indian summer monsoons are lovely. The showers give you a great opportunity to sip a glass of hot *chai* (tea) in your balcony, just watching the raindrops fall. But, there is a not-so-good side to it—infections! The rains also bring a host of bacterial and viral infections. Like every year, this year too, I was down with a nasty bacterial infection and was put on a course of antibiotics. Along with these, my doctor recommended antacids, which he said, would negate the side effects of the strong antibiotics known to cause acidity in the stomach.

It was time for dinner and I joined my parents, my uncle who was visiting us from the US, and my grandparents who were already at the table. My stomach started rumbling and I felt uneasy. My appetite was gone and my mom was quick to point out that I had a bout of acidity. I had forgotten my antacid and the strip of Zinetac lay untouched.

“You must be lazy enough to have forgotten to take your tablets on time. During our time, we could not even afford it”, my granddad remarked. I was stumped. What? “A strip of 10 tablets costs just about ₹ 5! And was it unaffordable a few decades ago?”, I sputtered. My eyes already had the expression clear enough for my dad to continue – “Well, it was not so back then. I remember, even until the 1990s, this strip was costing somewhere around Rs. 15 or 20<sup>1</sup>. Necessary medicines like these were quite expensive.”

Intrigued by this statement, I could not stop thinking how rich we were now, compared to then! “Hmm... Papa, you have now turned into a rich man”, I passed a snide remark. “Well, it is not that we became wealthy, it is just that the prices fell”, he quipped. My uncle, who was a silent witness to this conversation, chimed in, “Thanks to the generics drug market, many drugs have now become affordable. The US drug market is now almost taken over by the generic drug companies.”

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<sup>1</sup> [https://www.wto.org/english/tratop\\_e/trips\\_e/hosbjor\\_presentations\\_e/40love2\\_e.pdf](https://www.wto.org/english/tratop_e/trips_e/hosbjor_presentations_e/40love2_e.pdf)

That was the first time I heard the word “generic”. This story sounded quite interesting. I have always heard my parents and grandparents talk about how pricey things have become today. But here was a different story! Rather, going in opposite direction. My inquisitive mind did not stop questioning and I went back to my desk to find answers. After reading all the minute details written on its packaging, I found that this pill contained 150mg of ranitidine, a chemical that neutralises the acidity in my stomach, and was manufactured by a company called GlaxoSmithKline Pharmaceuticals Ltd in India. This was the oldest pharmaceutical company in India and was a subsidiary of GlaxoSmithKline plc, one of the world's leading research based pharmaceutical and healthcare companies.

Things became interesting when I later read that Indian pharmaceutical companies were now big players in the US market. How did they do that? After reading about the history, growth and successful business ventures of India's pharma majors, I promised to never look at any strip of tablets the same way again! It is a story of our competency in chemistry and chemical engineering and the determination of Indian companies to succeed, and never to look back.

## The generic drug market and advent of India's pharmaceuticals

Generic drugs are copies of branded drugs that have the same chemical composition or salt, intended for the same use as the branded drug and have similar effects, side effects, route of administration, risks, safety and strength as the branded drug. When a pharmaceutical company develops a new drug, it is usually granted a patent for the discovery and they become the sole manufacturers of that drug for about 20 years (in the US). Once the 20-year period lapses, any company can manufacture the same drug with the same chemical composition, and such drugs are called generics.

India has carved a niche for itself in the global pharmaceutical arena. Today, we have the second largest number of USFDA-approved manufacturing plants outside the US. India also has the largest inventories of highly skilled pharmaceutical professionals, competent enough to meet 95% of our domestic bulk drug requirements and the major requirement of drug formulations<sup>2</sup>. Drug prices in India are one of the lowest in the world.

The contribution of the pharmaceutical sector to India's GDP is 2%, and amounts to about 12% of the manufacturing sector GDP. During 2016-17, total pharmaceutical exports from India, including bulk drugs, were worth USD 16.4 billion. With an expected growth of 30% over the next three years, it is likely to hit a mark of USD 20 billion by 2020, according to the Pharmaceuticals Export Promotion Council of India (PHARMEXCIL)<sup>2</sup>.

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<sup>2</sup>India Brand Equity Foundation, Sectoral Report, January 2018, <https://www.ibef.org/industry/pharmaceutical-india.aspx>

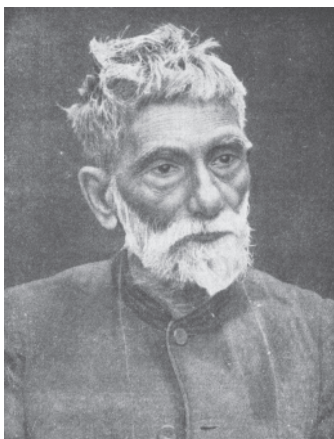
But this turn of tide is quite new and the Indian pharma sector received flattering spotlight just a couple of decades back. Along with Information Technology, the pharmaceutical sector has generated enormous capital and thrown up a record number of billionaires. Pharmaceutical exports are considered as the 'next big thing', and the sector is the fastest growing in the Indian economy after the global success of the IT industry.

## Historical origins of the Indian pharmaceutical industry

The pharmaceutical industry in India has its origins in the colonial period. Prior to the British rule, Ayurveda and Unani were the only indigenous forms of medicine practiced in India. The British introduced the European system of medicine to India in the 19th century, and owned most of the pharmaceutical companies that were established. However, there were no production units in the country. Raw materials were exported from India, and finished products were imported to the country.

On the other side, a surging nationalist thought gave rise to greater interest in science and technology, including the manufacture of chemicals and pharmaceuticals. The Indian Pharmaceutical Industry (IPI) came into being with the establishment of two firms. The first one was the Bengal Chemical and Pharmaceutical Works (BCPW), which was established in 1901 in Kolkata by the famed chemist, educator and entrepreneur, Acharya Prafulla Chandra Ray. P.C. Ray started his humble company at a rented house at 91, Upper Circular Road, Calcutta with a meagre capital of ₹ 700.00. Since its inception, Ray was very much quality conscious and produced various products that matched the British Pharmacopoeia standards.

The other one was Alembic Chemical Works Co. Ltd., established by Prof. Kotibhaskar, T.K. Gajjar and Rajmitra B.D. Amin, in 1907 in Vadodara, with the guidance and support of his Highness Maharaja Sayajirao Gaekwad. These two pioneering companies have withstood the test of time; they have risen and fell through crests and troughs of changing market dynamics, and still are the echelons of Indian pharma industry.



*Acharya P.C. Ray, Founder of BCPW. In Ray, the qualities of both a scientist and an industrial entrepreneur were combined and he can be thought of as the father of the Indian Pharmaceutical industry.*

(Photo Credit: By w:Prafulla Chandra Ray - <http://dli.gov.in/cgi-bin/metainfo.cgi/data14/upload/0029/794?&barcode=99999990338964>, Public Domain, <https://commons.wikimedia.org/w/index.php?curid=46240784>)



Around the same time, strong foundations of chemical engineering were laid out in India by way of its introduction in education. It was the foresight of the Late Dr. H.L. Roy, who introduced chemical engineering in the curriculum of the then Bengal National College, the nucleus of the present Jadavpur University, as early as 1921. Jadavpur has the distinction of conceiving and executing the first course in chemical engineering, even when this discipline was in its infancy in the developed countries of the West. From this early start, chemical engineering evolved in tune with the needs of the nation.

Following the footsteps of the Bengal National College (today's Jadavpur University), Punjab University in Chandigarh, Andhra University in Vishakhapatnam, Banaras Hindu University (BHU) in Varanasi, Calcutta University in Kolkata, the Indian Institute of Science in Bangalore and the University Department of Chemical Technology (UDCT) in Mumbai took an early lead by offering courses in chemical engineering and chemical technology.

The establishment of UDCT at University of Bombay was unique, as it was set up by industrialists and philanthropists; UDCT became the first department to get autonomy under the provisions of the University Grants Commission. Now called the Institute of Chemical Technology (ICT), it was started on 1st October 1933. Research has been an integral part of ICT since its inception and has created over 500 first generation entrepreneurs in chemical technology. The ICT grew significantly in stature ever since its establishment owing to its many contributions in the development of IPI and the dyestuff technology used widely in the textile industry.



*Institute of Chemical  
Technology (ICT),  
Mumbai*

*(Photo Credit: ICT Mumbai  
Facebook Page)*

In its early stages of development, IPI continued to remain import dependent, as most of the bulk drugs (the chemical molecules that give medicines their therapeutic effect) and formulations (the preparation of the final medical product) were imported. Only final packaging was done in the country. During the World War II, development of indigenous industry received an impetus due to the fall in the supply of imported drugs. As a result, Indian companies such as Unichem, Chemo Pharma, Zandu Pharmaceutical Works, Standard Chemicals, Cipla, East India Pharmaceutical Works, and others were established.

When India became an independent country in 1947, many multinational companies (MNCs) largely dominated the pharmaceutical market. Drug prices in the country were amongst the highest in the world. The bulk drug industry in India was in its infancy<sup>3</sup>. This made the great minds of the country to think of producing our own drugs for our own people. India's overall development strategy of import-substituting industrialization acted as the key driving force. The first two decades after independence saw a huge growth and expansion of the Indian pharmaceutical sector. But even then, the industry remained heavily dependent on imported technology due to the domination of MNCs, which retained most of the technical know-how. At that time, eight out of India's top ten pharmaceutical companies, based on sales, were subsidiaries of MNCs.

To remedy this, the Indian government, during 1950s, introduced policies stressing self-reliance through local production. It founded five state owned pharmaceutical companies to enforce this. The first public sector drug-manufacturing firm, Hindustan Antibiotics Limited (HAL), came into being in 1954 at Pune. It was established to produce antibiotics with help from the United Nations, the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF). Imported technology was then adapted to local conditions through its R&D wing to produce drugs. HAL was the first company in India to manufacture several important antibiotics such as penicillin, streptomycin, ampicillin and gentamicin.

Apart from HAL, few public funded research institutes, established under the guidance of the Council of Scientific and Industrial Research (CSIR), played a pivotal role in the growth of the pharma sector. Particularly, Central Drug Research Institute (CDRI) in Lucknow, the Indian Institute of Chemical Technology (IICT) in Hyderabad, the National Chemical Laboratory (NCL) in Pune and the Regional Research Laboratories (RRL) at Jammu and Jorhat. Nourished in a scientific environment, they evolved over the years to become a major force in the country's science and technology arena. Hundreds of technologies developed by these institutes have been transferred effectively from laboratories to industries over the last few decades.

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<sup>3</sup>Website of The Bulk Drug Manufacturers Association: <http://bdmai.org/about-bdmai/>



## National Chemical Laboratory (NCL), Pune

NCL was set up in 1950 with an objective to undertake research in the areas of chemistry important to the industrial development of the country, to collaborate with other scientific and academic institutions, and to develop technologies that could be commercially exploited by the Indian industry. Ambitious programs with special reference to heterocyclics, pharmaceuticals and pesticides were undertaken after 1965 under the leadership of Dr. B.D. Tilak, the then Director of the institute. Analysis, process improvement and the skilful use of sophisticated instruments have been NCL's forte. Pharmaceutical chemistry was one of the major component of NCL's research programs.

NCL's association with pharma industry dates to mid-1960s when products such as berberine hydrochloride, hexylresorcinol, 4-hydroxycoumarin, phenoxy-acetic acid, acetanilide, diethylstilbestrol, vitamin C, sorbitol, acriflavine, calcium hypophosphite, emetine, l-menthol, opium alkaloids and sodium cyclamate were manufactured by private industries based on technologies developed at NCL.

Allowing senior scientists to guide as many research students as possible in its formative years has resulted in NCL becoming a centre of excellence in all fields of



National Chemical Laboratory (NCL), Pune

(Photo Credit: <http://www.csir.res.in/gallery/national-chemical-laboratory-pune>)

chemistry and chemical engineering. The research groups in natural products chemistry under Dr. Sukh Dev and Dr. S.C. Bhattacharya brought international recognition to NCL and formed a backbone for qualified manpower for pharma sector.

Realizing the vital role that organic chemistry can play in the synthesis of drugs, emphasis was laid mainly on the development of technologies for various drugs and drug intermediates. With the able leadership of Dr. A.V. Rama Rao, Dr. N.R. Ayyangar, Dr. T. Ravindranathan, Dr. S. Rajappa, and Dr. M.K. Gurjar, the institute focused on finding new and innovative technologies that were cost effective too. NCL also encouraged drug industries to sponsor specific time-targeted and well-identified projects to develop manufacturing processes of those drugs that were either exclusively imported or insufficiently made in the country. The response to this program was highly encouraging, and during the course of time, many such projects covering a wide range of products were developed at NCL and successfully transferred to the drug industry.

NCL also provided the processes for the chirally active part of the drugs. Chirality is a geometric property of some molecules and compounds. A chiral molecule is non-superimposable on its mirror image. While synthesizing a known drug by a new route, NCL evolved novel approaches that offered economic benefits such as minimizing the number of reaction steps, avoiding handling of hazardous chemicals, and making the raw materials readily available.

NCL guided the Indian pharmaceutical industry in various ways in their formative years by providing institutional consultancy. Many NCL scientists were on the board of directors of a few pharma industries too. Today, they and are involved in identifying and funding research proposals for funding agencies like the Department of Biotechnology (DBT), Department of Science and Technology (DST), etc. Some of them are members of committees on regulating import duties, drug price control for pharma sector, accrediting in-house R&D units established by corporate industry, etc.

In 1958, the Government of India entered an agreement with the Soviet Union to manufacture antibiotics, synthetic drugs, and surgical equipment with an 80-million-Ruble loan. This led to the formation of the Indian Drugs and Pharmaceuticals Limited (IDPL) in 1962 in Hyderabad, with Soviet technical expertise. Shortly thereafter, many Indian-owned private pharmaceutical companies were established that upgraded and adapted acquired imported technology for local use by Indian chemists, scientists, and chemical engineers.

## Central Drug Research Institute (CDRI), Lucknow

CDRI was founded in 1951 with a vision to strengthen and advance the field of drug R&D in the country and to generate human resource for the IPI. The institute has made significant accomplishments in the pursuit of its mission to provide new drugs and technologies that translate to affordable healthcare for all, generation of knowledge base, and nurturing future leaders of the healthcare sector. Today, it is a modernized drug research in India having everything under one roof – from synthesis, screening, development studies, process up-scaling to clinical studies.

CDRI's contribution to IPI includes the discovery and development of 12 new drugs, of which, Arteether (Brand Name: E-mal), BESEB (Brand Name: Memory Sure), Centchroman (Brand Name: Saheli) are currently in the domestic market. CDRI has transferred more than 130 indigenous technologies to pharmaceutical companies that were successfully commercialized. So far, more than 10,000 research articles have been published by CDRI in peer-reviewed journals. It is conferred with more than 350 Indian patents and 90 international patents, and has produced more than 1000 Ph.D. scholars. Several of its alumni have today occupied highest positions in national and international academic institutions, biotech and pharma industries.



*Central Drug Research Institute (CDRI), Lucknow*

(Photo Credit: By Harshvardhansonkar - Own work, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=18050164>)

Despite these developments, due to the adverse economic situation, many private companies found it increasingly hard to survive, and eventually closed. The ones that survived the storm remained confined to production and packaging of drugs. Though some managed to formulate the preparation, they relied solely on imported bulk drugs and intermediates. This led to foreign pharmaceutical companies, including wholly or partly owned subsidiaries, rising to dominance. According to a Reserve Bank of India survey, for the period 1964-1970, MNCs had the most authority in the pharmaceutical sector, compared to other sectors.

## **Winds of change**

It was widely recognized that trade policy alone was inadequate to foster self-reliance in a process-driven sector. Continuous learning and technological capacity building was needed along with policies regarding intellectual property rights (IPR). The other priority was to reduce the cost of drugs and make them affordable to all sections of the society. Drugs were expensive not only because of the manufacturing process, but also because companies that held patents for a particular drug were monopolising the market and thwarting competition. Hence steps to address monopoly of IP rights were also necessary

When the pace of reform intensified in the 1970s, the Indian Patents Act, 1970 came as a big boost. The government decided to revamp the patent related laws to reduce the stronghold of MNCs and introduced the Indian Patents Act, 1970, that abolished product patents and adopted process patents, thereby promoting Indian companies to make generic versions of foreign made drugs. It allowed only process patents in the pharmaceutical products. The act enabled domestic pharma players to build their technical expertise in the reverse engineering of existing medicines by modifying the manufacturing process and thus, promoted efficient production of generic drugs. This brought costs down drastically, and medicines were made affordable. Regulation of the prices of bulk drugs under the Drug Price Control Order further encouraged the growth of pharma sector in India. This policy towards technological self-reliance and indigenization kicked off the golden era of the Indian pharmaceutical industry.

Reverse engineering, quite literally is taking apart an object to see how it works to duplicate or enhance the object. India's R&D capabilities lay in reverse engineering drugs and in process chemistry, and now companies could reverse engineer many drugs. The Indian economy responded well to the new changes and the sector grew by leaps and bounds. Many multinational drug manufacturers eventually abandoned the Indian markets as they could not match India companies in providing drugs at such low prices. With their exit, indigenous companies rushed in to fill the void and flourished thereafter. By 1990, India became self-sufficient in the production of formulations (finished medicines) and nearly self-sufficient in

the production of bulk drugs. Today, India is one of the biggest producers of generic medicines in the world, and our pharmaceutical sector is known as 'the pharmacy of the third world'.

Many companies took advantage of the provisions in the Indian Patent Act of 1970. One such company, Cipla, decided to take on the world's most powerful corporations. The company 'copied' the out-of-patent anti-AIDS drug and sold it at dirt-cheap rates to the poor by 2001.

### Cipla – The torchbearer

Cipla was founded by Dr. Khwaja Abdul Hamied as 'The Chemical, Industrial & Pharmaceutical Laboratories' in 1935 in Mumbai. The name of the company was changed to 'Cipla Limited' on 20<sup>th</sup> July 1984. In the year 1985, US Food and Drug Administration (FDA) approved the company's bulk drug manufacturing facilities. It was during 1959-60, Dr. Yusuf Hamied, son of the Cipla founder, joined the company as a young scientist. A Cambridge-educated chemist, Hamied led the company to become a global icon for its role in defying foreign MNCs to provide generic drugs to treat under-privileged people in developing countries.

Known to use his chemistry notebooks from Cambridge when he developed new syntheses of drugs, Dr. Hamied shot to fame when he told a European Commission meeting at Brussels that he could sell a three-drug anti-retroviral combination for the treatment of HIV AIDS for \$800 per patient per year. This caused uproar because Western pharmaceutical companies were selling the same combination for \$12,000 per patient per year. This happened at a time when the HIV/AIDS epidemic was at its peak in Africa. Millions of Africans were dying due to lack of affordable medicine. Poor African countries, which were big consumers of these medicines, welcomed the Cipla offer. Cipla was highly successful in the market and soon dropped prices to less than a dollar per patient a day.



Dr. Yusuf K. Hamied  
(Photo Courtesy: IISER Pune)

Dr. Hamied's contribution to saving millions of lives included reverse engineering complex drugs to manufacture them for a fraction of the price and reformulation to combine multiple drugs into single pills making them easier to take. The resounding success of Cipla can be summed up from a quote by Dr. Yusuf Hamied that appeared in the magazine *Business Standard*, "More than eight million Africans are treated with the Cipla drug. In India, the price difference between a multinational and a Cipla drug can be gauged by the fact that the latter today sells a



stomach cancer drug for ₹ 6,500 for 30 tablets against ₹ 2.8 lakh charged by multinational competitors.”<sup>4</sup>

Cipla, thus, set a benchmark and brought about a revolution in the country. It was the first purely indigenous company that started manufacturing generic drugs in India. The phenomenal growth of the Indian pharmaceutical industry can be seen through the fact that in a relatively short period, seven Indian pharma companies including Cipla and Lupin are now worth more than a billion dollars.

## Achieving the impossible

A combination of well-planned government policies, availability of trained manpower through public educational institutions, and the public-sector enterprises, created conditions favorable for the pharmaceutical sector to flourish in independent India. The change in India's patents regime in 1970 favoring process patents gave rise to dozens of pharmaceutical companies. The government focused its attention and resources on creating a portfolio of niche companies for which the required work force was already available in the country. This served as a new source of sustainable competitive advantage for the Indian pharmaceutical sector during the 1990s.

The public-sector enterprises and academic/research institutes played a significant role in enriching the human capital endowment that was necessary for the pharmaceutical sector of the country to flourish. Founders of almost all the major Indian pharma giants (about one-third of the 200 large companies) have worked in the production or the R&D wing of IDPL (Indian Drugs & Pharmaceuticals Ltd.) at some point or the other.<sup>5</sup> These founders acquired the necessary skills required for reverse engineering through their long-term associations with the public-sector unit and they played a fundamental role in the new product and process development.

“A shining example is Dr. Anji Reddy of Dr. Reddy's Laboratories who worked at IDPL during his early-career days. He then went on to become an entrepreneur post-1970. Thus, besides drugs, IDPL also created entrepreneurs”, says Padma Vibhushan awardee Prof. Man Mohan Sharma, who worked as a Professor for 33 years and later served as the Director at ICT (formerly UDCT), Mumbai.

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<sup>4</sup>Chatterjee, D. 40 years ago... And now: Cipla: The crusader for affordable drugs takes the patent battle to MNCs. *Business Standard* December 24, 2014

<sup>5</sup>Mazumdar, M. (2013). Performance of Pharmaceutical Companies in India: A critical analysis of industrial structure, firm specific resources, and emerging strategies. Physica-Verlag Heidelberg.

### Kallam Anji Reddy

Born as the son of a turmeric farmer in Andhra Pradesh's Guntur district, Reddy graduated in Pharma Technology from ICT. After finishing his PhD in Chemical Engineering from the National Chemical Laboratory (NCL) Pune, he started his career with Indian Drugs & Pharmaceuticals Ltd. (IDPL) in 1969. He quit IDPL in 1975 and became part of two partnership firms for the next nine years. In 1984, he set up Dr. Reddy's Laboratories (DRL) with an initial capital of ₹25 lakhs and served as its Chairman. Today, DRL is a doyen of the Indian pharmaceutical industry.



(Photo Credit: By Tashif - Own work, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=16961986>)

Scientists-turned-entrepreneurs brimming with intellectual excitement and the drive to make it big, thrived during this period. "Technocrat entrepreneurs flourished in the country at that time," remarks Prof. Sharma.

Another stalwart in the Indian pharma industry is Dr. Alla Venkata Rama Rao (Dr. A.V. Rama Rao) – a scientist and entrepreneur who was successful in taking pharma research to the markets. He is the only Fellow of the Indian National Science Academy (FNA) who has trained 112 Ph.D. students, published more than 250 papers in reputed international scientific journals and developed over 30 process technologies for manufacturing affordable, life-saving drugs. After retiring as the Director of IICT Hyderabad, Dr. Rao built a multi-million-dollar pharmaceutical company called Avra Laboratories that currently has over 550 employees.

In 1973, based on a directive from CSIR, Dr. Rao developed a novel process for manufacturing diazepam, an anti-anxiety agent used worldwide. During that period, he met Dr. Y.K. Hamied of Cipla, who immediately showed keen interest in commercialising this process. This marked the first example of a CSIR technology transfer to the industry and its successful commercialisation.

**A.V. Rama Rao** was born and brought up in Guntur town of Andhra Pradesh and graduated in chemistry in 1956 from A.C. College. After working for two years as demonstrator and technical assistant at A.C. College and Agricultural College, Bapatla, he joined ICT in 1958 for his graduation in chemical technology with specialization in

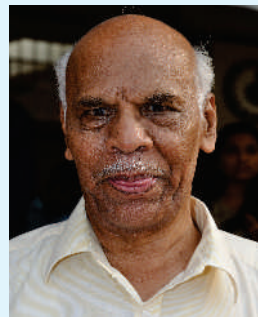


pharmaceuticals and fine chemicals. He continued his career as a Ph.D. student at NCL under the guidance of Prof. K. Venkataraman, the then Director of NCL, and obtained his Ph.D. degree in 1964.

Unlike many who go abroad to pursue their post-doctoral career, Dr. Rao followed Prof. Venkataraman's advice and stayed at NCL working on the structure of lac dye—an age-old problem unsolved for almost hundred years. He was offered the position of Scientist B at NCL in 1965. For the next seven years, he pursued academic research.

Dr. Rao was selected as the Head of the Organic Chemistry Division at NCL in 1980. He established the first school of excellence for the synthesis of bio-functional molecules such as anti-tumour antibiotics, immunosuppressants and cyclic peptides including vancomycin. Later, he moved to Hyderabad in 1985 as Director-RRIL and transformed it into a globally respected IICT.

Dr. Rao was the first Indian scientist to take lead in integrating basic sciences, technology development and engineering design to provide a complete package for commercial exploitation. He was also instrumental in pioneering the concept of institution and industrial interaction with several leading pharmaceutical industries such as Cipla, Lupin, Cadila, Dr. Reddy's, FDC etc. He was also responsible for developing alternative affordable technologies for several essential drugs including anti-HIV drugs, which enabled the pharma sector to introduce them to the market at a fraction of the prevailing international price (from: BioSpectrum (India), April 15 2016).



*(Photo Credit: CC BY 3.0  
(<http://creativecommons.org/licenses/by/3.0/>), via Wikimedia Commons)*

The story of another Indian pharma giant, Lupin, is on the same lines. Founded by Desh Bandhu Gupta, who started his career as an Associate Professor at the Birla Institute of Technology and Science, Pilani, Rajasthan, quit teaching and decided to be an entrepreneur as he was "not able to implement ideas into practice". He came to Mumbai and worked in a small British pharmaceutical manufacturing company. He founded Lupin in 1968 with a start-up capital of ₹5000, borrowing the money from his wife. Named after the Lupin flower because of its inherent qualities and what it personifies, the company was created with a vision to fight life-threatening infectious diseases and to manufacture drugs of highest priority. The first

office of Lupin—a rented premises in central Mumbai—was used for dispatching medicines. Later, with a loan of ₹8 lakhs from the Central Bank of India, D.B. Gupta started a factory whose major order was to provide iron and folic acid tablets to various programs by the government related to maternal healthcare. Under his leadership, Lupin became a global pharmaceutical company and is now a leader in manufacturing anti-TB drugs and lisinopril, a chemical used in the treatment of hypertension.

A remarkable achievement of the Indian pharma companies was their ability to produce active pharmaceutical ingredients (APIs) – the basic component of the drug. “New age scientist-cum-entrepreneurs in India came out with the concept of manufacturing and then exporting active pharmaceutical ingredients (APIs). The Western world today is dependent on India and China to get their supply of APIs. This big change has occurred since the inception of the Indian pharmaceutical industry”, says Prof. Sharma.

About forty years ago, India started exporting APIs at affordable prices, which kick-started the generic drug revolution in India. Many pharma companies in the country pursued research and development on APIs and new chemical entities (NCEs). Interestingly, a lot of horizontal transfer of technology, from one company to the other, took place with respect to not only global patents, but also those filed by fellow Indian companies. “I don't see that happening in other sectors in India as easily as it happens in pharma. This is another feather in the cap of the pharmaceutical sector”, mentions Prof. Sharma.

Thanks to these factors, the cost of production of drugs in India is today 35-40% lower than that in the US<sup>6</sup>. Another factor largely responsible for India's dominance in the pharma sector is the huge pool of skilled chemists and chemical engineers in the country. Indian chemists have been able to control the inventory through their own ingenuity to reduce the manufacturing and distribution costs. Labor costs are 50–55% cheaper and the cost of setting up a production plant in India is 40% lower than that in the Western countries. With sustained contributions from scientists, chemists and chemical engineers, the pharma industry is now a hot pick.

“Can one imagine how an industry could expand to USD 20 billion in merely three to four decades? If we did not have the work force to feed the growing pharmaceutical industry, it would not have been able to flourish this well,” says Prof. Sharma.

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<sup>6</sup>Jadia, V. 6 ways in which India has managed to keep the costs of generic medicines very low. *The Better India* April 9, 2016.

### **Who are 'chemists' and how different are they from 'chemical engineers'?**

Often confused between the two, chemists work with relatively small amount of chemicals in a laboratory bench. They are found developing new drugs or testing different chemicals in a laboratory. They tend to focus on developing novel materials and processes, analyzing substances, measuring the physical properties of substances and testing theories.

Chemical engineers, on the other hand, work on industrial scale reactions with factory size equipment. They are constantly looking at how to scale drug production or manufacture a drug commercially with various industrial processes in the play. They are likely to take new ideas, products, and turn them into more useful and efficient products so they are cheap and made widely available. Most of their work falls into the design, manufacture, and operation of plants and machinery, and the development of new materials or substances. Chemical engineers focus on making products for profit and on a large scale.

India's skilled workforce in the pharma sector is today better than most of its peers' in Asia and other developing countries. With institutes like ICT churning out a large number of passionate and skilled graduates in all levels of competencies, workforce was never a challenge. Now, ICT has opened doors for several new disciplines of chemical technology, pharmacy and biotechnology, which have played a paramount role in building the pharmaceutical industry in the country. Most of the professional bodies of the technocrats of these disciplines, even today, operate from the portals of excellence of ICT.

The industry is expected to generate 58,000 additional job opportunities by the year 2025.<sup>7</sup> Presently, over 80% of the antiretroviral drugs used globally to combat HIV/AIDS are supplied by Indian pharmaceutical firms. What makes India the world's largest producer of generic drugs is our affordable R&D strategy, innovative and reliable products and the sustained collaboration between the academia and industry.

“Culture plays a very important role in shaping people's perceptions and actions. Intangibles such as hard work, perseverance, and goodwill of our scientists, chemists, and engineers were like a boon for our approach to innovation and quality”, emphasizes Prof. Sharma.

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<sup>7</sup>India Brand Equity Foundation, Sectoral Report, January 2018, <https://www.ibef.org/industry/pharmaceutical-india.aspx>

## M.M. Sharma

The contributions of the academicians, like that of the entrepreneurs, are paramount too. Prof. M.M. Sharma is a legend himself, who has made strides in chemical engineering. Considered as an institution in himself, he has contributed to pharmaceutical industry and the government on matters vital to the growth of science and technology, and the nation at large. Recollecting his association with ICT (formerly UDCT), Prof. Sharma says, "It is a long story! I was a young man of twenty-seven when I became a Professor. We were just three or four faculty members and had no money for research. It was a challenge. As engineers, we were trained to look for solutions rather than focus on problems. I decided to start from completely idea-oriented research, which requires negligible money. After 1970s, I did not have enough PhDs to supply because the demand had become so high!"

Prof. Sharma's innovation not only reflected in publications in learned journals, but also in the quality of his teaching. "If I were to use the language of Biology, I would say that right from the beginning, we had the right DNA. Our motto was very clear. Our first emphasis was on teaching, then research and then consulting. Our linkage with the industry has been exemplary right from very early days", he says with pride. Stalwarts like him did a great job of transforming uncut stones into polished diamonds.



(Photo Courtesy: IISER Pune)

Today, India's growth as the generics manufacturer has turned to benefit our own people in a big way and is poised for extensive domestic market reach. Recently, the Government of India, under the aegis of Department of Pharmaceuticals, has launched the Jan Aushadhi scheme under which there are thousands of generic drug stores operating across the country. The idea is to ensure that the poor and under-privileged section of the



A Jan Aushadhi Centre in Nagaur district of Rajasthan  
(Photo Courtesy of Down to Earth)

population get affordable medicines. These drug store chains provide low-cost, affordable, generic medicines manufactured indigenously. The government, in partnership with small and medium manufacturers, has promised to continue the supply chain's momentum in producing low-cost, high-quality generic medicines for domestic consumption.

When I finished my research on the massive growth of the Indian pharmaceutical industry, I could not but stand in awe and appreciation for the numerous dedicated scientists, researchers, entrepreneurs, academicians, policy-makers and lawmakers who made it all possible. We can now take pride in the fact that we are a 'drug sufficient nation', who is now generously contributing to the cause of saving lives. I am mesmerised! Aren't you?

## Acknowledgements

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# THE INDIAN PHARMACEUTICAL INDUSTRY (IPI)

## 2017: AN OVERVIEW



Third largest in terms of volume (accounting for 20%), and thirteenth largest in terms of value, in the world



Largest provider of generic drugs globally, accounting for 20% of global exports in terms of volume



Over 80% of antiretroviral drugs used globally to combat AIDS come from Indian pharmaceutical firms

Estimated to grow over 15% between 2015 and 2020, to US \$55 billion

Branded generics constitutes nearly 80% of the market share



Accounts for around 30% by volume and about 10% by value in the US generics market



100% FDI allowed in the pharmaceutical industry



Pharma exports to the US to get a boost in FY18, as branded drugs worth US \$50 billion will become off-patented

Private equity and venture capital (PE-VC) investments in the sector have grown at 38% year-on-year between January-June 2017



The Government of India unveiled 'Pharma Vision 2020' aimed at making India a global leader in end-to-end drug manufacture





## Growing greens in glass: Plant tissue culture technology

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*By Kavita Tiwari*

Though the heat was as scorching as it would be on any morning in May, today was different. Ramakrishnayya and Radhamma, a farmer couple and owners of 'Venkateshwara Farm' in Duvvur, Andhra Pradesh, arrived in a new car. While Ramakrishnayya carefully parked the car on the side of the road, Radhamma gushed with pride. The dream of owning a car, something that they never thought possible, was now a reality.

Things were not the same a decade ago. Ramakrishnayya and Radhamma, then in their thirties, left their hometown in Guntur district to explore new livelihood. With a loan of one lakh rupees, they started a small nursery in Duvvur, and stayed in Kadapa, Andhra Pradesh. Their routine 34 km travel from Kadapa to Duvvur used to be in a state-run bus that zoomed on the dirt-laden roads. The nursery, however, was a delightful sight. They cultivated and sold seedlings of mango, banana, coconut and spices, to farmers in the locality. For five years, they ran this venture without much technical expertise, relying on methods they had learnt from their parents.

It was all good until trouble came in the form of diseases that affected the seedlings and killed many of them. This resulted in huge losses and five years of hard work in their two-acre nursery was washed away. Desperate, Ramakrishnayya turned to the nearest Krishi Samruddhi Kendra, an agricultural extension centre established to provide support to the agricultural sector, for help. Explaining the perils of running a nursery without the required training, experts at the Krishi Samruddhi Kendra suggested setting up a tissue culture nursery instead.

Motivated to change their own fortunes, Ramakrishnayya and Radhamma attended a month's training programme in plant tissue culture techniques at the Gandhi Krishi Vigyan Kendra (GKVK), Bengaluru. With some financial assistance, Ramkrishnayya launched his new plant tissue culture (PTC) laboratory in their two-acre land. This venture was successful in producing 150 to 200 microplants (plants grown from tissue culture) from a single part of the plant—seeds, seedlings, cuttings or other plant materials—in just about 6-7 months.



The couple were exhilarated! The sleepless nights, hard work, and dedication had paid off. The new plants were ready for sale in a short span of 6-7 months, which would have otherwise take a year or two! They soon started transferring the new plants into poly bags to sell them off.

Soon, what was once a small, ordinary nursery had now transformed into a thriving and ever-growing beautiful homestead. Today, the farm also has three greenhouses (poly houses or shade houses) to ensure production of high quality planting materials of uniform grade, in all seasons, throughout the year. The farm also generates employment for many in the locality – of the 33 labourers employed, 15 are skilled staff and 18 are unskilled. Today, the farm is run on a professional scale.

At a time when farmer suicides continue unabated due to the agrarian crisis in the country, the story of how a 51-year-old farmer defied all odds and set record yields in producing banana and mango plantlets is an inspiring story indeed. Ramakrishnayya is now a role model for those aspiring to venture into a financially viable, self-employment enterprise. Today, he is helping many farmers like him, to grow plantlets using plant tissue culture in over 200 hectares of land in the neighbouring districts.

This story isn't just Ramakrishnayya's triumph against adversaries, but a part of a larger victory of plant tissue culture. The Plant Tissue Culture or PTC, practiced widely in the nursing and farming industry, is a robust technique for mass production of many plants. Here, a new plant can be grown from any part of the plant; it need not be a fruit or seed!

So how does PTC work? Plant tissues, also called explants, are collected from selected high yielding varieties, or mother plants, and cultured in a medium of known composition under sterile conditions. It is then induced to divide and develop into a complete plant. This method allows producing large number of new plantlets, unlike a traditional nursery that is dependent on seeds alone. Plant tissue culture has a major contribution in meeting the ever-increasing demands of new plants in the field of agriculture, forestry, horticulture and medicine.

The market in India for plants grown through tissue culture was estimated at ₹500 crore for the year 2016, according to a report by the Department of Biotechnology (DBT). India has around 200 tissue culture companies operating commercially. These companies can produce about 500 million plantlets per annum. PTC is universally acknowledged to be one of the most original and vital tools for direct application in agriculture. Since its inception, PTC has greatly contributed to the production of food, feed, fibre, and fuel, and has emerged as a commercially viable tool to rapidly produce high-quality and disease-free plants that give a high yield irrespective of the season of the year.

Today, farmers like Ramakrishnayya across the world produce plantlets of banana, potato,

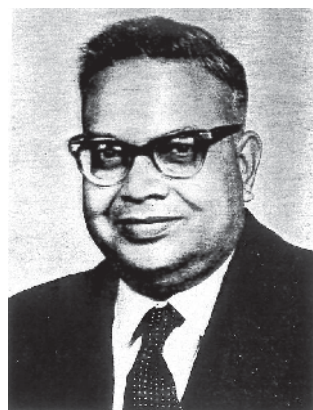
sugarcane, apple, pineapple, strawberry, gerbera, anthurium, lillium, orchids, bamboo, date palm, teak and pomegranate, with tissue culture. In spite of this, not many farmers are aware about PTC.

But when did this all start? The history of PTC can be traced back to a time 70 years in the past, roughly around 1947. The time not only marked the beginning of a new era for India, but a triumph for a small group of botanists (plant scientists) who set out to attain new heights of scientific glory in plant sciences. This is a fascinating story of how growing plants in a test tube changed the landscape of agriculture.

### Early development in embryology

Prof. Panchanan Maheshwari, rightfully called the “Father of Modern Embryology” laid the foundations of plant tissue culture in India. A student of Ewing Christian College, Allahabad University, Panchanan learnt the basics of botany under his Professor Dr. Winfield Scott Dudgeon. He then worked in Agra College, and moved to Dacca University where he did his research on embryology.

For a long time, scientists and common man had known just one way of how plants reproduced – through pollination. Most plants that we grow can be classified into self-fertilized (by the fusion of pollen and ovule of the same flower) or cross-pollinators (wherein pollens fuse with the ovules of flowers of another plant). The ovules are then fertilized and an embryo, which we know as the seed, is formed. When the environment is suitable, this embryo grows into a plant. The study of this entire process is called 'Embryology'.



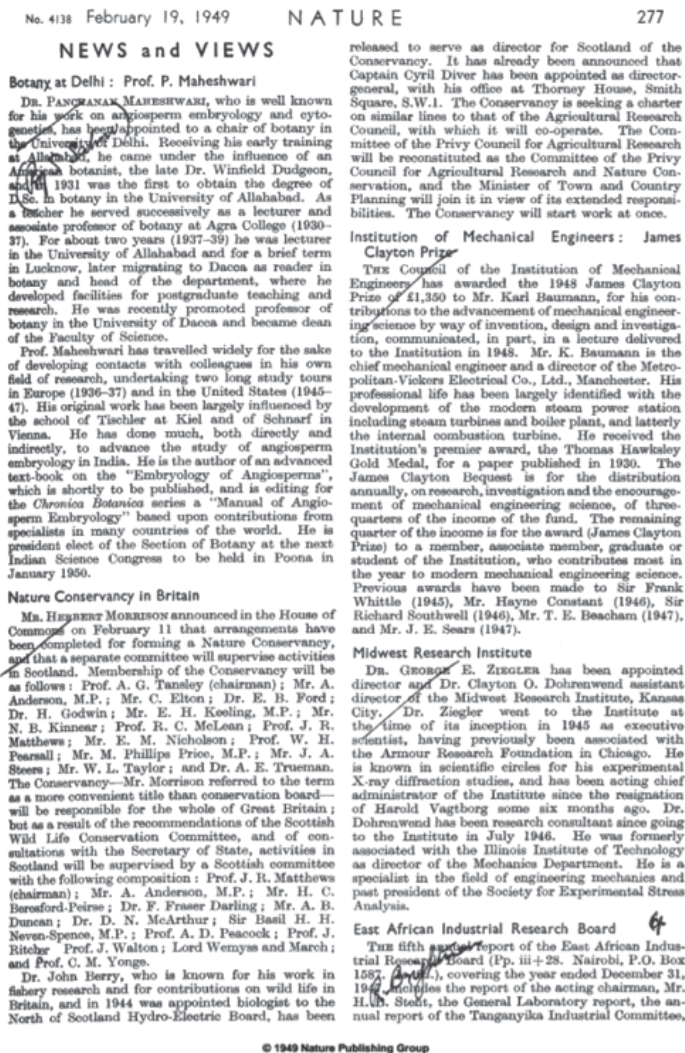
*P. Maheshwari*  
(Photo Courtesy: Current Science)

After India became independent and the country was partitioned, Dr. Maheshwari, who was in Dacca – the then East Pakistan, came back to India and joined the Delhi University as the Head of the new Department of Botany. Here, he and his student Brij Mohan Johri, led various research activities and the group soon became internationally recognised. Students were encouraged to carry out experiments and the scientific fervour was such that even undergraduate students made new discoveries.

Dr. Maheshwari's stay in Delhi turned out to be the most creative and productive period of his career. Even now, since the last six decades, no other institution has surpassed the

Department of Botany at DU, as a centre of research in embryology and tissue culture. University Grants Commission (UGC) later recognized the department as a Centre of Advanced Studies in Botany.

In the early 1960s, Dr. Maheshwari and his students became interested in *in vitro* fertilization (artificial reproduction) of flowering plants. In flowering plants, the process of fertilization takes place deep inside the flower, so it is difficult to experiment or make detailed observations. Experimental embryologists since long wanted to make possible *in vitro* fertilization in plants similar to that achieved in animals. Dr. Maheshwari's research group created a major breakthrough when they achieved fertilization in a test tube after pollinating the cultured ovules. As this opened up the possibilities of *in vitro* cross-fertilization of genetically distinct strains, the technique opened new avenues to plant breeders to quickly test hybrids.



Snapshot of a special editorial on Prof. Maheshwari titled "Botany at Delhi: Prof. P. Maheshwari" published in the prestigious journal *Nature* in the year 1949.

Important discoveries in the history of PTC in India	
1958	Scientists are able to regenerate somatic embryos in vitro from the nucellus of Citrus ovules (P. Maheshwari and Rangaswamy)
1960	First successful test-tube fertilization in Papavaraceae and Brasicaceae (K. Kanta and P. Maheshwari)
1961	Successful establishment of the technique of test-tube fertilization of angiosperms (P. Maheshwari)
1963	Developed continuously growing callus cultures from mature endosperm of <i>Santalum album</i> (Rangaswamy and P.S. Rao)
1963	First successful callus culture of Pinus established (R.N. Konar)
1963	Demonstration of the division and proliferation of mature endosperm cells in <i>Ricinus communis</i> (Mohan Ram and Satsangi)
1964	Haploid Datura plants produced from pollen grains and successful anther culture for the first time (S. Guha and S.C. Maheshwari)
1965	Production of full triploid shoots by culturing a mature endosperm of a root parasite, <i>Exocarpus cupressiformis</i> (B.N. Johri and S.S. Bhojwani)

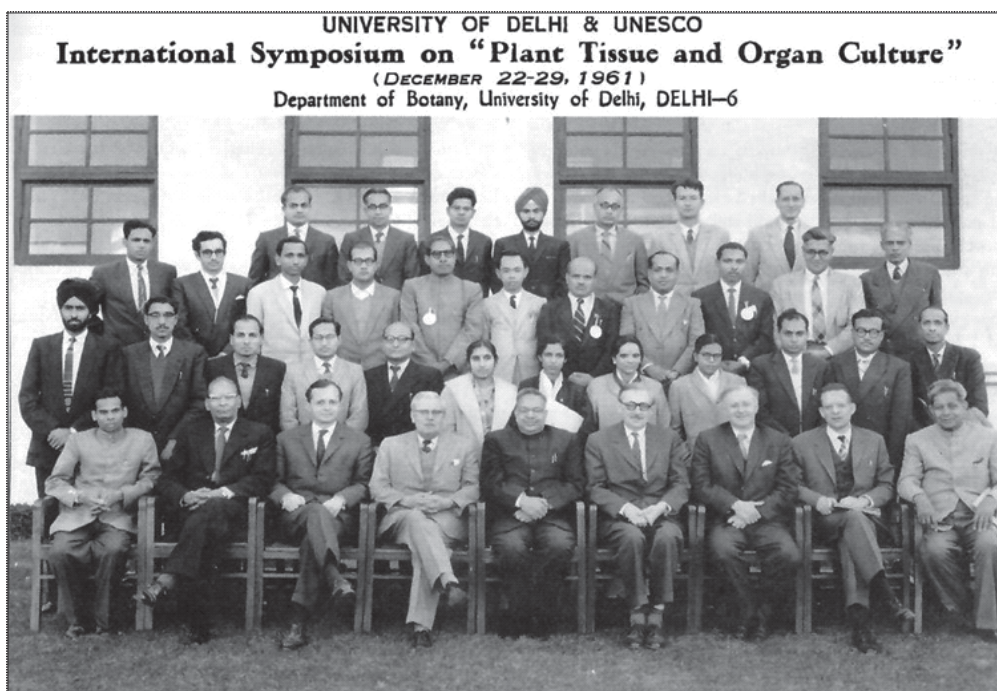
## Development of Haploid Plants

Among the many who have contributed to India's journey in plant tissue culture, the name Prof. Shipra Guha-Mukherjee stands out. Dr. Mukherjee did her Ph.D. on tissue culture of onion under the guidance Prof. B.M. Johri in Delhi University. During those days, plant breeders across the world were conducting extensive research to develop haploids—plants with cells that have a single set of unpaired chromosomes. During her post-doctoral research during 1964-66, Dr. Mukherjee developed the technique of producing haploid pollen plants using anther culture with Prof. S.C. Maheshwari. In 1964, the duo used the excised anthers of Datura plant to directly develop haploid embryos and plantlets from the microspores. She later collaborated with Dr. M.S. Swaminathan, the then Director of Indian Agricultural Research Institute, and the Father of Green Revolution in India, for raising haploids in rice. This technique provided an opportunity to generate genetically identical population of plants of a particular strain of crop, which was essential in any plant breeding programs. What used to take years to make a variety isogenic (still which was never truly isogenic), it took just one or two generations to generate truly isogenic strains. Thereafter, much progress has been made in developing anther culture of wheat, rice, potato, maize, pepper, and a wide range of economically important species.



## Haploid Plants

All living organisms are composed of cells, the smallest unit of life. Cells divide and reproduce in two ways – mitosis and meiosis. The cells produced from meiosis are called haploids because they contain only half the number of chromosomes present in a normal cell. A chromosome is a DNA molecule with part or all the genetic material (genome) of an organism. Haploid plants are of great significance in producing homozygous lines (homozygous plants) and for genetic improvement of crops. Homozygous lines have identical pairs of genes for any given pair of hereditary characteristics. The importance of haploids in the field of plant breeding and genetics was realized long ago, but nothing substantial could be done to raise haploid plants. Pollen and anther, the part of a flower that produces and stores pollen, are good materials for raising haploids.



*A rare group photograph taken during one of the many symposiums organized at the Department of Botany, DU for imparting training in plant tissue culture and experimental embryology. It shows, sitting from left to right: N.S. Rangaswamy (Convener), B.M. Johri, J. Reinert, F.C. Steward, P. Maheshwari, J. Swarbrick, H.E. Street, J.P. Nitsch, and B. Sen. (Photo Courtesy: Prof. H.Y. Mohan Ram, who is standing at the extreme left in the last row)*

After the development of pollen embryo culture by Dr. Maheshwari's group, another major development that triggered the rise of PTC research in India was micropropagation – where propagation is done through plantlets grown in tissue culture and later planting them out. Prof. Narayanswamy at the Bhabha Atomic Research Centre, Prof. H.Y. Mohan Ram, Prof. N.S. Rangaswamy, and Dr. K.R. Shivanna at Delhi University were a few names that initiated the early work in the field of micropropagation. This was much needed to reduce the time between two generations of plants and to increase the number of progeny per plant. The techniques thus developed for *in vitro* propagation of plants allowed strong and continued growth of PTC industry in the country.

The science of all these techniques (in vitro fertilization, another culture, micropropagation) and the new science that was studied using these techniques revolutionized Botany all over the world and lead to a whole new era of Plant Tissue Culture (PTC). As you could see, Indian scientists have played a major role in developing PTC, which has contributed immensely to address the problems of food and nutrition all over the world.

### **The journey towards commercialising PTC**

While stalwarts like Dr. Maheshwari, Dr. Johri and others were meticulously researching in Delhi, Dr. V. Jagannathan at the National Chemical Laboratory (NCL), Pune, started a new school of research in PTC. The school, first of its kind in the country, put NCL firmly on the world map in the field of biological research. After Dr. Jagannathan, one of his students Dr. A.F. Mascarenhas, took his work to greater heights and was instrumental in defining a business model around PTC.

The efforts of NCL towards PTC starts with a fascinating story of Ram and Laxman, two 100-year old teak trees in the Allapalli forest of Gadchiroli district in Maharashtra. The trees were unique in that they were termite and disease free, had wide girth and would yield good quality wood. However, they were too old to regenerate their parts. Several attempts to propagate trees like these by officials from the Maharashtra Forest Development Corporation (MFDC) failed. That is when they approached NCL for help, in 1975-76.

The quest to propagate trees such as Ram and Laxman in large numbers initiated meristem tip culture in India. Meristem is newly formed tissue consisting of actively dividing cells and found mainly at the growing tips of roots and shoots. Scientists from NCL proved that it is possible to grow plants in the laboratories from the tissues of mature trees. Thus, NCL became the birthplace of successful mature forest tree tissue culture in the world. Later, as per the demands of the forest department, meristem culture was applied to other important trees like eucalyptus, *Salvadora* etc.

NCL could achieve the herculean task of producing 1,000 teak plants in their laboratory for MFDC. These plants were grown at different locations across Maharashtra from 1978 to 1980. Teak plants produced at NCL not only survived then, but are also standing tall even today. Meristem based propagation of teak and eucalyptus, both plants of economic importance, brought huge commercial profits. The work done at NCL established the fact that plant raised through tissue culture could be successfully transplanted in the field.



*Tissue culture raised teak trees still standing tall since they were planted at the NCL campus, Pune around 1975-76, symbolizing the hard work of our scientists (Photo Courtesy: Dr. Kavita Tiwari)*

For NCL scientists, success brought additional responsibilities and soon, they got involved in another major project. Around that time, eucalyptus farming was a boom and many of the small farmers were diversifying towards its plantation. What was needed to take this further was large number of plants from a known high quality species of eucalyptus. Tissue culture was already an established technique for producing quality plants of major trees and crop plants. The next step was making the micropropagation process cost-effective and beneficial for use in forestry programs across the country. Scientists at NCL worked on two species of eucalyptus as a part of a project funded by the National Bank for Agriculture and Rural Development (NABARD), who aimed to help poor farmers of the country through this ambitious project.



Other than eucalyptus, the team at NCL also worked on *Salvadora persica* – pilu (पिलु) or meswak (मिसवाक) in Hindi – a plant that grows along the seashore in the Gulf of Cambay. Oil from fruits of *Salvadora* is used as a substitute for coconut oil in the soap industry and people living in the surrounding villages depend on the oil for their livelihood. Increased soil salinity had rendered the area unfit for cultivation. Recognizing the economic importance of this tree, one company came forward to identify a variety of *Salvadora* that could grow well even in the saline soil. They provided superior quality strains of *Salvadora* to NCL for its large scale production without losing its genetic features - the best way is using tissue culture methods of cloning and production.

During the process, the scientists at NCL developed an indigenous technology for cloning *Salvadora* species. Thousands of plants were produced and supplied to the local community. These plants, raised from a superior mother plant, gave birth to baby plants that showed faster growth patterns and could be easily multiplied on a commercial scale. *Salvadora* promoted overall wetland development of the barren land of Kutch by providing poor rural households with a sustainable living. This technology of cloning was later transferred to the Central Salt & Marine Chemicals Research Institute (CMCRI) in Bhavnagar, Gujarat.

The plants produced at NCL soon found widespread acceptance across the country. NCL immensely contributed towards establishing different tissue culture laboratories across the length and breadth of India and in providing training to the local people and research personnel.

## **Raising commercial crops through PTC**

Inspired by the success of PTC in growing plants of eucalyptus and *Salvadora*, work on producing major crops like cardamom, turmeric, banana, ginger and sugarcane was under progress at NCL. This time, the scientists used standardization of callus regeneration and clonal propagation methods to achieve their objectives.

Callus is a growing mass of plant cells or soft tissue that forms over a wounded or cut surface, leading to healing. It is an unspecialized, unorganized, growing and dividing mass of cells. Callus is capable of regenerating into a whole plant. Clonal propagation refers to the process of asexual reproduction by multiplication of genetically identical copies of individual plants.

It was during the mid 1980s that tissue culture caught the attention of entrepreneurs in the country. Around 1984-85, A.V. Thomas & Co., a Kerala based company, kick-started the era of commercialization of tissue culture crops in India. Cardamom tissue culture technology was the first ever tissue culture technology to be licensed to any company in the country by NCL.

A.V. Thomas & Co. started large-scale production of cardamom in a commercial unit. They adapted the bench scale protocol developed by Dr. R.S. Nadgauda and Dr. A.F. Mascarenhas at the Department of Biochemistry, NCL. Soon, other companies followed suit. The Indo-American Hybrid Seed Company started a second unit in Bangalore in 1988. Today, many companies such as Hindustan Lever, Tata Tea, Unicorn Biotech, Nath Seeds, RPG Enterprises, Indian Tobacco, and Hindustan Agri Genetics Limited are working in the field of micropropagation in the country.

Despite all the technological advancements, NCL still faced a major limitation in reaching out to the farmers. The process used for in the laboratory to raise tissue culture plants needs to be modified for commercial production. In 1989, DBT came up with a new proposal that aimed at establishing a tissue culture pilot plant at NCL that could adapt the processes to commercial production. A pilot plant having a simple design was then established at NCL using an indigenous technology. This cost-effective and state of the art commercial lab soon become a model project for many tissue culture companies in the country. Later, it was upgraded to a Micropropagation Technology Park (MTP) to help entrepreneurs, industries, institutes and universities to produce plants at a large-scale. NCL next decided to expand its horizons into horticulture species and crop plant based research. The Micropropagation Technology Park worked towards aiding the interaction of the industry with the end user group. Soon the farmers become aware of the benefits of using the tissue culture technology.

Within few years of its establishment, the tissue culture plant at NCL produced more than ten lakh plants of forestry species and provided them to farmers, forest departments, and forest corporations across the country. Our scientists not only innovated on the protocol of these technologies to make them more cost-effective, but they also came up with new methods of plant regeneration with proven perfection to take it to the commercial level.

Development of several new species of food crops, trees, cereals, vegetables, flowers, oilseeds, and plantation crops such as spices, coffee, tea, and rubber has been possible because of tissue culture. Plants raised through tissue culture have uniform harvest time, faster growth, and exceptionally high yields. It would not be wrong to say that the awareness generated among farmers by scientists at NCL paved the way for the mass acceptance of the tissue culture raised plants in the country. Tissue culture research has completely revolutionized farming in India today. These techniques are extremely popular for propagation of various cash crops, flowering shrubs, trees, and for germplasm conservation. Germplasm is the raw material – seeds or tissue from leaf, stem, pollen or cultured cells – that can be grown into a mature plant. More than 1.4 billion plants have been produced by NCL alone and planted at 350 locations across India ever since.

Scientists at NCL earned their spurs across continents by sharing their wisdom of forest tree tissue culture with foreign counterparts. Dr. Shuchishweta Kendurkar of NCL, who worked on micropropagation of teak plants, recalled how a 35-year-old UK based tissue culture company once approached NCL to obtain the teak tissue culture technology. This was the first transfer of technology from a developing country to a developed country. The UK based company entered into a second license agreement with NCL for expanding their business venture and for setting up pilot plants in Indonesia and Australia. This technology developed at and owned by NCL, is also apt for production automation.

### **Express blooming in bamboo**

Another breakthrough that won international acclaim for the team at NCL was flowering of tissue cultured bamboo plants. Bamboo is known to flower after very long intervals in the order of tens of years, and the entire bamboo population from the same origin flowers simultaneously.

Scientists at NCL developed a technique that made it possible for the first time for three species of bamboo plants to flower within weeks, against several years taken by plants that grow in the wild or are raised by conventional methods. Bamboo flowering was achieved by growing seedlings from mature tissues in a special nutritious jelly containing a plant growth regulator. This innovation presents many firsts. It was the first time a consistent *in vitro* flowering of bamboo was achieved. Botanists could now easily produce bamboo hybrids to yield better quality bamboo. Additionally, this was the first scientific contribution from India on which the prestigious journal, *Nature*, published a special editorial.

The news took the world by a storm. No one had ever thought that this technology would excite such a furore among the scientific community. Known to have numerous important economic implications given the vagaries of flowering pattern in bamboo, the team's success in developing seedlings that can flower in just three cycles of transferring is of immense importance. Under natural conditions, these seedlings could have taken 30 years to grow, that too without flowering. This technique was of considerable significance to developing countries, where bamboo holds significant potential to contribute to the global forestry resource deficits. Since then, bamboo has emerged as an important substitute for wood and fibre.

NCL has also contributed to standardization of meristem tip culture technique for getting virus-free plants for sugarcane, and clonal propagation and callus regeneration for turmeric.

## Conservation of rare island orchids

Tissue culture technology has empowered many poor farmers of the country. But the most successful commercial achievement yet of plant tissue culture in the country, according to Prof. H.Y. Mohan Ram, an eminent botanist and a student of late Prof. Maheshwari, is the conservation of rare orchids from North East India way back in 1983. In 1995, the Jawaharlal Nehru Tropical Botanic Garden and Research Institute (JNTBGRI) at Palode, Kerala, initiated an intensive breeding program with a view to tap the potential of rare species and genera of orchids. This not only helped in the conservation of a near-extinct species, techniques our scientists introduced for their large scale production brought commercial success. The conserved rare species included those with ornamental as well as medicinal value

## The next big step

The potential of PTC to revolutionize the growth of agriculture in India was clear. The Department of Biotechnology (DBT) established the National Certification System for Tissue Culture Raised Plants (NCS-TCP) in 2006. It aims to mentor the tissue culture companies for production and distribution of disease-free and high-quality plants raised through tissue culture. The NCS-TCP has given recognition to 96 companies and accreditation to 5 test laboratories and 2 referral centres, since its inception. Around 80 million tissue culture plants have been certified through this system till date. Moreover, no major disease outbreak has ever been reported in the country in the last 10 years.

Tissue culture laboratories in the country are also multiplying horticultural plants. Year over year, more and more farmers are using poly house horticulture. Farming and agroforestry offer a lot of opportunity for use of tissue culture technology. PTC is no more an infant industry in India; it is estimated to be flourishing with multi directional growth and multimillion-dollar turnover in the years to come. Several crops like anthuriums, bananas, strawberries, sugarcane, orchids, carnations, etc. are widely propagated using PTC, which are traded domestically and internationally for nearly three decades now.

But, the most amazing aspect of this success story of plant tissue culture in India is the indigenous grooming of scientists and researchers that endeared them all to the country. Tireless and lifelong efforts on their part promoted the large-scale application of PTC, inspired new generation scientists, and stimulated the development of scientific activity based businesses in the country. Prof. S.C. Maheshwari, a distinguished plant scientist and son of Late Prof. Panchanan Maheshwari rightly quoted the importance of PTC, "The genetic engineering technology would not have been there but for plant tissue culture".

Today, we are all set to showcase our technical prowess on the international arena by generating substantial earnings from technology transfer. The widespread application and adoption of PTC by our farmers can be greatly attributed to the cost-effectiveness and indigenous technological innovations by our scientists. Over last few decades, an increasing demand for agricultural, forestry, plantation and horticulture crops has created an increased demand for high-quality, high-yielding and disease-free planting stock. Research in PTC technology has undoubtedly brought about the second green revolution in our country.

This story of scientific innovation with a built-in purpose to improve crop yield and the lives of farmers and the general population has touched the lives of many like Ramakrishnayya, who can now be freed from the shackles of traditional agricultural practices. Many, like Ramakrishnayya, can now benefit from the profits PTC has brought to their coffers, thanks to the passion and dedication of our scientific community. Now, all Ramakrishnayya can think about is the bushel of mangoes and bananas in his farm, and what it means to him and his family.

*Note: While Ramakrishnayya and Radhamma are fictional characters, they represent large number of farmers who have benefited from Plant Tissue Culture—a revolution in agriculture.*

## Acknowledgements

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# 7

# Steps of Plant Tissue Culture

1

## Selection of Plant



An organ, tissue or a cell obtained from cells, callus, anther, pollen or embryo of a parent plant and used for *in vitro* culture in aseptic conditions is known as an 'Explant'.

2

## Isolation, Inoculation & Sterilization of Explant



Explant culture

3

## Incubation



4

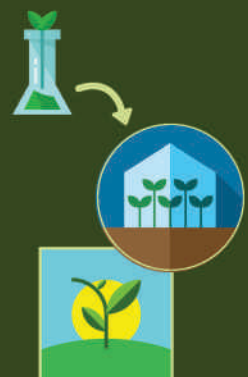
## Initiation of Callus

Plant callus is a growing mass of unorganized parenchyma (fundamental tissue) cells



7

## Transfer of Plantlets



Once rooting takes place, the plantlets are transferred to a Green House or an open field

5

## Sub-culturing



Callus separated and single cells cultured

6

## Regeneration & Hardening



Further culturing generates new plants



## **Amul: India's story of the white revolution**

*By Kavita Tiwari*

For nine-year-old Asma, the chilling winters of the Kashmir valley, her home, is bittersweet. She loves the snow that the winter brings and likes to snuggle under her blanket, but nothing more. The valley, famous for its breath-taking and beautiful summers, has a story of plight during the winters.

Winters in Kashmir often lead to heavy snowfall and landslides resulting in roadblocks. The valley, in many cases, is cut-off from the rest of the country, unsettling the day-to-day lives of the Kashmiris. There is severe disruption in the supply of essential goods – fresh vegetables and fruits dwindle in supply and fresh milk is out of reach. The Kashmiris endure this season by surviving on a humble meal, lacking most of the nutrients needed.

For Asma and the many of her age, the lack of fresh milk affects their nutritional needs. The calcium in milk, necessary to develop strong bones, is crucial for children of that age. During winter, the disruption in the milk supply hits the children the hardest. Their only savior is a magic portion of a white powder mixed with water that their mothers prepare with love. This is the humble 'milk powder' available in the next-door grocery shop. It is quick to prepare, compensates for the lack of fresh milk, and tastes somewhat closer to milk.

The packet reads – “Amulya Dairy Whitener.” If you turned the packet around, there is this famous name “Amul – The taste of India.”

For many, 'Amul' is not just a name, but an emotion that is associated with sweet memories – the smell of Amul butter on freshly baked bread, the single-lined pun of the advertisements, the famous mascot 'Amul girl' and so on. Amul has become a household name for the last 50 years or more.

But little does one know how a small milk union that started in Gujarat, is now ruling our kitchens with a wide variety of milk and milk products. Its technological innovations now light up the lives of many like Asma in the country. This is the story of India's home-grown 'white



revolution' – a revolution that transformed India from a milk-deficient nation into a milk-sufficient one.

This story does not have a single hero. Each of the hundreds of scientists, veterinary doctors, marketing managers, dairy technologists, extension workers and thousands of farmers have contributed to this in their own way. It was an effort weaved together with grit and determination when India was just born. This story is a grand example of the fact that it is not just the final product that defines a brand, but also the collective effort towards continuous innovation that is behind it. Here is a reflection on the arduous journey of a tiny firm striving to be the 'Taste of India'.



A collection of Amul products (Photo Courtesy: Pranali Y. Patil, Abhijit Bhagat)

## Prelude to a milk cooperative

In 1924, when India was still occupied by the British, many British people residing in Bombay (the present Mumbai) fell sick after consuming spoilt milk. The then government looked into every nook and corner for better sources of milk, and in 1926, zeroed in on Polson Dairy. Polson was the only existing dairy back then, and it was given the monopoly to collect milk from Kaira district in Gujarat and supply it to Bombay.

The Polson dairy was founded by Pestonjee Edulji Dalal, who known with the nickname Polly. A British sounding 'Polson' sounded good as a brand name, so he chose that. The dairy would receive milk supplies from the farmers of Kaira, where the small town of Anand is situated.

Polson's major challenge was keeping the milk fresh for the 360 km distance between Kaira and Bombay. To keep the milk fresh, the milk cans were packed in gunny bags and cold water was poured on them. Bombay thus became the primary customer for the milk suppliers of Anand. Pestonjee, the ambitious entrepreneur, created the BMS or Bombay Milk Scheme that was aimed at betterment of farmers. However, the pricing of the milk was arbitrary and the traders and agents of Polson dairy stated exploiting the milk producers who operated on very narrow margins.

In 1945, the built-up anger amongst the Kaira farmers led them to approach Sardar Vallabhbhai Patel, under the leadership of the local farmer leader Tribhuvandas K. Patel. Sardar Vallabhbhai Patel was the President of the Gujarat Pradesh Congress Committee then. This necessitated a revolution in marketing the farmers' produce in a way that would benefit the farmers. The idea was to putting the farmers in charge of procuring, processing and marketing of milk. Patel suggested that the farmers sell their produce directly to the BMS, and bypass Polson, by establishing a co-operative union.

Soon, the farmers set up their own milk cooperative union. In retaliation, Polson began finding fault with the quality of the cooperative's milk. Thwarted, the farmers went back to Patel who suggested that the farmers start owning dairies to end dependency on Polson. Morarji Desai, the then Minister of Home and Revenue in Bombay proposed the idea to form a society for collection of milk in a meeting held at Samarkha village near Anand, on 4<sup>th</sup> January 1946. He insisted that BMS accept milk directly from the Kaira farmers instead of the one supplied by Polson.

However, this plan failed. BMS was not ready to buy milk directly from the cooperative. In protest, the farmers went on strike. It lasted for 15 days and became famous later as the milk strike of Kaira. They poured milk on the streets, and refused to give a single drop to Polson. Polson's milk collection came to a standstill and BMS collapsed. Dara Khurody, the Milk Commissioner of Bombay at that time, convinced the British to concede and BMS agreed to accept milk directly from the Kaira farmers.

The newly formed co-operative thus got initial success. The farmers wanted Tribhubandas Patel to be the Chairman of the Kaira co-operative, even though he admittedly knew nothing about the dairy business. Thus the small, sleepy town of Anand saw the establishment of the Kaira District Milk Producers' Union. The Union was formally registered on 14<sup>th</sup> December, 1946.



*One of the early milk production units of Amul*  
(Photo Courtesy: Amul Dairy)

### The sleepy town of Anand

Anand could be fairly called the sleeping beauty of Gujarat that woke up to life with the white revolution. Back in 1945, it was a slow little town, situated 101 km from Gandhinagar. Now, it is the 'milk capital of India', full of life. The city is home to the Head Office of Gujarat Cooperative Milk Marketing Federation Ltd (parent organisation of Amul), the National Dairy Development Board of India, a well-known business school, Institute of Rural Management Anand (IRMA), and the Anand Agricultural University.

### Anand – The centre stage of India's milk production

Post-independence, the Kaira cooperative had a different set of challenges to face. The soaring population of the country placed a high demand on dairy products. Like other food products, the supply hardly met a fraction of the demand. The need for the hour was to somehow increase the output of milk and milk products.

But, the domestic dairy industry had its own inefficiencies and challenges. Seasonal rainfall affected the availability of green grass for the cattle. Barring a couple of months when it rained, the cattle were mostly fed with crop residues unfit for human consumption. This often

led to the tremendous drop in milk production during the dry season and milk became a scarce commodity. This severe shortage had its direct impact on the nutritional demands of growing children – the next generation in the making.

### **The unfolding of the 'white revolution'**

It was 1949. A metallurgy engineer by choice and a dairy engineer by chance, 28-year-old Verghese Kurien was sent by the Indian government to its run-down, experimental creamery at Anand in Gujarat. With a small salary of Rs. 275, a rather uninterested Kurien set out to Anand. Hailing from Calicut, he had completed his masters in metallurgy and dairy engineering from the Michigan State University, USA.

Forced to stay in Anand due to a bond signed with the Government of India, Kurien initially disliked Anand. His workplace was dull, with the staff of hundred plus whiling away their time with the hope that someday the headquarters at Bangalore would decide to close this unit. Verghese tried resigning, but his request was promptly rejected.

#### **Life before Amul**

Verghese Kurien completed his engineering from a college in Guindy and wanted to join the army. His mother, aghast over the loss of her husband in the army, tore up Kurien's military commission letter for the Army's Electrical & Mechanical Engineers (EME) wing. Instead, he was directed to work for TISCO (Tata Iron and Steel Company) where his uncle John Mathai, a director at TISCO, had organized an apprenticeship for him. The ingots and molten iron of Jamshedpur could not retain Kurien for long, as his heart was not in it. He sought ways out.

In 1945, the British government announced a scholarship program for aspiring Indian students to study overseas. With the intention to do a master's programme in metallurgy or nuclear physics, in spite of opposition from family and his uncle, Kurien applied for it. He needed to appear for an interview in front of a board headed by Sir Maurice Gwyer of Delhi University.

When he thought he was living his dream, a shock came in the form of a question that asked him what he knew about pasteurization. Based on whatever he could recollect, he mentioned that it was something to do with boiling milk at a certain temperature. Maurice readily announced Kurien's selection for a course in dairy engineering. Kurien attempted a meek protest, but was informed that it was the only seat left. With a heavy heart, he accepted the scholarship and started to plan his journey to the USA.

After spending the next few months preparing for the course at the Imperial Dairy Institute at Bangalore, Kurien landed at Boston. When he went to the Ohio State University, he realised that he had been misdirected. Redirected to the Michigan State University, he studied under Prof. Arthur Farrell. There he completed a degree in metallurgy with nuclear physics and dairy engineering as his minors. During his stay in USA, Kurien was also trained at one of Wisconsin's creamery plants.

While in Anand, Kurien was introduced to Tribhuvandas Patel by Maganbhai Patel, a bureaucrat famous for land reforms. During the time, Tribhuvandas and his Kaira milk cooperative were struggling to prevent the spoiling of milk and milk products processed using the equipment in the government creamery. Antiquated machinery of the creamery would often fail, and Dara Khurody in Bombay would reject the milk supplied to them. Kurien helped with the repairs of the out-dated machines, which kept the creamery at Anand running. Milk soon began to be pasteurized and chilled before being supplied to Bombay.

One day, an irked Kurien finally told Tribhuvandas in resentment that if they wanted to survive, they should buy new equipment. And soon he found himself in Larson and Toubro (L&T) Bombay to buy a pasteurizer, which he did for Rs. 60,000, an amount that was given to him by Tribhuvandas.

On his return to Anand, Kurien attempted to seek relief from his bond again. This time, much to his surprise, the request was granted! Kurien joyously began preparations to leave but Tribhuvandas was upset and distressed with this decision. He wanted Kurien to stay as his presence was important for the Kaira cooperative to function efficiently.

After much discussion, a grieved Tribhuvandas requested Kurien to continue for two more months at a salary of Rs. 600 per month. His plea was simple – *"We need you here!"*

*"Kurien says that it was these four words that held him to Anand for the rest of his life. He just could not leave them in despair. Was it his respect or friendship with Tribhuvandas, was it his conviction to doing something worthwhile or was it something else? Kurien says that he was gradually pulled deeper and deeper into the workings of the cooperative and the day-to-day life of the farmers.*

*He says – "I saw that when you work merely for your own profit, the pleasure is fleeting, but if you work for others, there is a deeper sense of fulfilment and if things are handled well, the money too is more than adequate."*

– Excerpts from Maddy's Ramblings Blog, India's milkman - Kurien and Amul



Once Kurien decided to stay, the next step was to name the products from the Kaira cooperative and make it a household brand. K.M. Philip, Kurien's brother-in-law, was instrumental in sensitizing Kurien to the needs of having a clear marketing strategy. He stressed the importance of creating and popularizing the brand. So, what would the name be? After a brainstorming session, the suggestion from a chemist who worked in the dairy laboratory was accepted. The name was to be 'Amul', derived from the Sanskrit word 'Amulya', meaning priceless. With a 'swadeshi' flavour, the Anand Milk Union Limited, popularly known as Amul, was born in 1957.

But it wasn't just Kurien who created what is today the largest cooperative movement in the history of the world. The merit also goes to the farmers who showed their willingness to associate together for their produce, and to be led by young professionals while retaining the ownership. And of course, the innumerable contributions from other characters in this story of revolution, as we shall soon see.



*One of the famous Amul cartoons  
in honour of Verghese Kurien  
(Image Courtesy: Amul Dairy)*

## The problem of plenty

During the summer months when the milk supplies were irregular, BMS would import milk powder from New Zealand. The powder was reconstituted into liquid milk to meet Bombay's milk demand. This gave some clues to the farmers of Kaira to start manufacturing milk powder when milk was in plenty, and use it during the lean summer months. However, most of the milk from Kaira came from the buffaloes, and the technology to produce milk powder from buffalo milk was not yet available.

### Indian buffaloes

Buffalos are mainly found in the Indian continent and are known to give more milk than cows. Besides, they can be fed low-quality feeds or coarse fodder such as wheat and paddy straw, sugarcane tops, or the residue that remains after extraction of oil from groundnut, copra and mustard-seeds and yet give ample milk. Buffaloes are more beneficial than cows because most of the farmers cannot afford costly feeds or set aside land for intensive forage cultivation. Also, buffaloes are not fussy eaters like the cows that need their food fortified with toppings such as jaggery. Buffaloes, thus, have always been a simpler and safer option for the poverty-stricken farmers of India.

### Technovation: The advent of indigenous milk powder from buffalo milk

Resolved to manufacture their own milk powder, the Kaira farmers consulted a panel of experts in the dairy industry only to hear that milk powder could not be made from buffalo milk. This was because buffalo milk was too thick, had 15% more proteins than cow's milk, and high amounts of fat.

In the process of making milk powder, water is made to evaporate from milk, resulting in condensed (thick) milk. This is then converted into milk powder by spraying it in a very hot air chamber. In the case of buffalo milk, this step is a challenge because the viscous buffalo milk would jam the nozzles. If the nozzle holes were made bigger, then the temperature in the chamber would have to be increased to dry the milk drops, as the drops would be bigger. The proteins in milk would lose their properties at such high temperatures and the resulting powder would not dissolve properly in water. But, if the temperature was low, the powder would not form at all. This made converting buffalo milk into powder, an arduous task.

Soon, Kurien went to New Zealand check if he could find a way to make milk powder from buffalo milk. While in New Zealand, he discovered by chance that New Zealand was selling substandard milk powder to India. When confronted, it offered to reduce prices and promised to support the development of dairy technology in India. New Zealand was then the largest producer of milk powder in the world, but they used only cow milk. They did not have buffaloes. Switzerland, the second biggest producer of milk powder also did not have buffaloes. In spite of the international support, the challenge to make milk powder from buffalo milk remained unsolved.

The tides turned when the milk conservation division of UNICEF (United Nations Children's Fund) was looking for partners to help the FAO's (Food and Agriculture Organization) campaign to eradicate hunger and malnutrition in Indian children. UNICEF came to know that Bombay was supplied milk from Kaira district, and offered to donate milk-drying equipment



worth Rs. 8,00,000, if the government agreed to distribute, through BMS and Amul, Rs. 12,00,000 worth of free milk to undernourished children in Kaira. Amul now had the money to invest on the technology to produce milk powder.

Another major breakthrough to Amul's efforts in this phase came in the form of H.M. Dalaya, a dairy engineer and Kurien's friend from the Michigan State University, who also studied dairy engineering. Kurien persuaded Dalaya to join him at Amul. Intrigued by the 'milk powder' challenge, Dalaya started experimenting with his ideas using a small experimental milk powder plant at Larsen & Toubro's factory. He was keen on acquiring it for Amul. But, before he could initiate talks in this regard, he was told that it had already been sold to one Teddington Chemical Factory at Andheri, Mumbai. Dalaya and Kurien managed to locate the company and persuade its manager to loan them the machine. With this second-hand powder-making machine, Dalaya successfully demonstrated to UNICEF that making milk powder from buffalo milk was indeed possible! After this, UNICEF decided to fund their proposed powder plant.

Dalaya later visited Denmark to study milk powder plant designs and operations. All these efforts culminated in the development of a spray dryer called 'Niro Atomizer' within a year. Finally, Amul developed the world's first sprayer-dryer designed explicitly for buffalo milk.

That was the panacea for the problem of plenty. Now, farmers no longer had to be scared about 'milk holidays' or periods of surplus/deficient milk. In 1955, Amul completed setting up a plant to manufacture milk powder and butter, with financial assistance from UNICEF, the governments of New Zealand and India.

This invention also gave an edge to Amul to compete successfully with Nestle, which used cow's milk to produce milk powder. Later, research by Dr. G. H. Wilster, a well-known cheese researcher, led to cheese production from buffalo milk at Amul. Soon, Kurien took over the reins of established competitors like Aarey dairy and the Polson dairy, and firmed his grip in the Bombay market.



*The Amul trinity: Tribhuvandas Patel flanked by Verghese Kurien and H.M. Dalaya*

*(Photo Courtesy: By Source (WP:NFCC#4), Fair use, <https://en.wikipedia.org/w/index.php?curid=55227773>)*

## Baby food – The next big leap with CFTRI

Post-independent India was parched, quite literally, with the onset of droughts in many parts of the country. As a result, the country's Forex reserves fell. Although the dairy industry was making steady progress, it was still far from feeding a growing population comprising a large number of infants aged between 1 and 1.5 years. Until 1960, India met its entire requirement of baby foods through imports, burdening the already lean foreign exchange reserves. Also supplies of baby food were short and erratic, resulting in shortage and soaring prices of baby food.

The obvious solution was to produce indigenous baby food and reduce our dependency on foreign brands like Glaxo, Demex and Lactogen. Now, the dairy engineers at Amul started thinking if this would be an opportunity to seize. Here again, all imported brands used cow's milk to produce baby food, and substituting that with the country's surplus buffalo milk was a challenge. Although dairy engineers at Amul had invested huge efforts to crack this puzzle, they could not make much headway. That is when Kurien approached the Central Food Technological Research Institute (CFTRI), a pioneer in food technology, in Mysore.

### A snapshot of Central Food Technological Research Institute

A constituent laboratory of the Council of Scientific and Industrial Research (CSIR), CFTRI came into existence in 1950 with the great vision of pursuing research and development in the areas of food science and technology. The focus of the institute has since been on using low-cost technologies, indigenous raw materials and bio-friendly processes to achieve food safety, health and nutrition for all.

Buffalo milk posed similar challenges to the plan to manufacture baby foods, like it did in the case of milk powder. Being rich in fat, buffalo milk is difficult to digest for babies and indigestion can often lead to diarrhoea. Now, the challenge was to remove this excess fat to make it suitable for babies. But then, what to do with the removed fat? This set everyone thinking.

Engineers from Amul worked on certain enzymes, compounds that speed up chemical reactions, to remove the excess fat in buffalo milk. Milk was churned using a modified equipment, to separate out the fat, and the remaining low-fat milk was collected separately. A team of scientists at CFTRI fabricated an innovative spray dryer that had hot air inlets at the bottom to dehydrate the fat, and convert that into a solid powder. This powder had an extended shelf life than milk, and could be kept for as long as six months at room temperature if unopened. The skimmed fat found its way into other by-products.

Thus, India's first indigenously manufactured baby food was the result of culmination of ideas from the best engineers at Amul and the top scientists at CFTRI. With this, the world witnessed yet another success story of achieving the impossible within the limits of time, technology, and resources. The baby food, thus developed from buffalo milk, was licensed only to Amul and was marketed under the name 'Amulspray Instant Milk Food.'



*Amulspray's classic advertisement and Amulspray cans*

*(Image Courtesy: Amul Dairy)*

An illustrious team of scientists like Dr. M.R. Chandrashekhara, Dr. P.K. Ramanathan, Dr. M. Swaminathan, and Dr. V. Subrahmanyam from CFTRI worked on the success of Amulspray. They displayed tremendous commitment and passion – sleeping in the pilot plants for days and missing their meals. “It was the passion and compassion of our scientists to work with an integrated approach without any hesitation or reluctance, that made this a reality”, says Dr. V. Prakash, ex-Director at CFTRI, acknowledging the support of farmers and engineers from Amul, and the Indian government.

Thanks to these home-grown innovations, Indian buffaloes soon became the talk of the town. ICAR (Indian Council of Agricultural Research), CSIR and ICMR (Indian Council of Medical Research) started working towards increasing the production of buffalo milk. They initiated programs covering topics from animal husbandry to welfare of cows and buffaloes. Realising that the health of the animals was a top priority if we were to increase milk production, Kurien emphasized that veterinary doctors visit local farmers instead of the animals going to them. This spared the farmers from taking each animal to the doctor and instead, every animal was monitored for its health by veterinarians.

“It was like a push to the nation from all angles. Our success became viral”, recalls Dr. Prakash. “Apart from uplifting the lives of rural people through the creation of mass employment, the Indian dairy industry improved the economic and nutritional status of every Indian. There was no looking back”, he points out.

But, the challenges to baby food did not stop there. Conducting clinical trials, an important aspect to ensure that the baby foods were safe to use, was not easy. How would one persuade a mother to feed her child something that she is unsure of? On the other hand, the baby food was a great substitute for human milk, and could save the life of an infant who could not be breast-fed. CFTRI cracked this marketing dilemma by educating mothers about the product, its benefits, and its usage. Mothers were welcome to visit the laboratories at CFTRI too. In fact, it wasn't the babies that tasted the baby foods first; it was team who developed it!

An additional challenge lay in using the baby food. Unlike human milk, baby food does not come as 'ready to use'; it must be prepared with water. Due to the high rate of illiteracy prevalent during that time, not many mothers understood how to prepare it. In addition, clean drinking water was scarce, and consuming baby food mixed with contaminated water would result in diarrhoea. Scientists then advocated the need for boiling the local pond water, and sterilizing the bottles to prevent nasty infections.

In 1958, Amul expanded their factory to manufacture sweetened condensed milk. They added a new wing after two years, which they used to manufacture 2500 tons of roller-dried baby food and 600 tons of cheese per year. This was the first time that cheese or baby food was made from buffalo milk on a large, commercial scale, anywhere in the world.

"Using science, our scientists have been able to develop low-cost innovative technologies that gave a boost to productivity in agriculture and push to the markets. Those were the days when we learnt to do things ourselves", recalls Dr. Prakash.

This was the moment of glory for India's reliance on its scientific community.

## Beating the global competition

After Amul was registered as a brand, it launched its own butter. New Zealand's Anchor butter and Polson butter were two well-established brands in the Indian market. How would a new local brand displace these?

Kurien, in his book, mentions how Amul did it:

*"A person came to our dairy and after having met me, said that if I needed any help from him, I can ask for it anytime. That was T. T. Krishnamachari (TTK). He was a businessman initially, before he went on to become a politician and subsequently a minister. So, once we got his blessings, I wrote him a letter saying, 'Would you cut the import of butter by 25 percent?' he wrote back, 'As desired by you, I am ordering a cutback of 25 percent.' No discussion, no meetings, no files, nothing..."*

*After six months, I wrote him another letter saying, "I am making more butter, and can you cut the import by 62.5 percent?" He wrote back, "As desired by you, I am ordering a cut of 62.5 percent." Then, after some time, he wrote informing me of the foreign exchange crunch and said that he is ordering a 100 percent cut in imports. "Please make sure that the nation faces no shortage of butter; I leave that job to you." That was the end of the matter."<sup>2</sup>*

## All the goodness in a plastic pack

The green revolution of early 1960s had not only enhanced the availability of grains, but also increased straw and other by-products used for cattle feed. This led to white revolution increasing milk production at Amul. This also necessitated newer modes of transportation of the milk so that more people, particularly children, had access to their daily nutrition.

Packaging is the vital link in the entire chain of production, storage, transportation, distribution, and marketing of milk and its products. Efficient packing not only leads to optimal use of resources, but also protects the contents against spoilage and its associated health hazards.

When Amul first started, milk was sold door-to-door and the containers were often handled unhygienically. At times, there was the possibility of adulteration where water and other harmful ingredients were mixed with milk. Hence, the need for tamper proof packaging was paramount to consumer convenience and safety.

In the West, milk was packaged either in Tetra Pak, a solution by Sweden based packaging company, or in HDPE (High-density polyethylene) injection blow moulded bottles. Plastic pouches are single-use packages, very light, easy to distribute and transport, and cost a fraction when compared to glass bottles. Losses during filling are also lesser than bottles.

However, until 1973, people in India bought milk in returnable glass bottles. In 1974, a team from Indian Petrochemicals Corporation Limited (IPCL) championed the replacement of glass bottle with LDPE (Low-density polyethylene) sachets for milk packaging. It was Dr. Varadarajan, the then Chairman of IPCL, who asked his team as to why they couldn't package milk in flexible packaging. This was an absolutely new thought at that time in India.

"Incidentally, when I joined IPCL, I did not know how blown films were made of LDPE. Yet, Dr. Varadarajan had no difficulty in asking me to work in a team led by marketing and product application folks to develop the concept", recalls Dr. S. Sivaram, ex-Director at NCL (National Chemical Laboratory), and one of the team members who worked on this ambitious project, in an article he wrote to his colleagues on the death of Kurien. "This was also my first introduction to learning the technology of plastics, which took me back to textbooks for education", he adds.

India's first LDPE plant was commissioned in 1975 at IPCL, Baroda. The team then took the proposal to Amul and met Kurien. Within a few meetings, Kurien was convinced. The first aseptic continuous sachet filling line was commissioned in Anand in 1976 using sachets made from 'Indothene' from IPCL.

"Glass bottles for milk was confined forever to the dustbin of history", says Dr. S. Sivaram, adding that if not for the revolutionary packaging concept, the 'white revolution' may not have been a reality. "Just imagine the fuel needed to transport 120 million metric tons of milk, the scale of milk production in 2011, in glass bottles by road and what a load on the environment it would have been!", he says.

Today Amul has a wide range of packaging solutions, from LDPE sachets to long life ultra-pasteurised milk available in an EVOH-based 5-layer film (LLDPE/LDPE). It also has adopted the Tetra Pak packaging for some of the products.



*Amul's long life UHT milk, Amul Moti, can stay fresh until 90 days without refrigeration.*

*(Photo Courtesy: Pranali Patil & Pratik Salve)*

## The grand finale

The story of India's white revolution, where farmers took it upon themselves and gained the courage to dream, to hope, and to live, goes on. The small milk cooperative of the Kaira farmers has become the Gujarat Co-operative Milk Marketing Federation Ltd. (GCMMF), jointly owned by 3.6 million milk producers in Gujarat. India has become the world's largest producer of milk and milk products. Amul is the largest food brand in India, with exports to more than 60 countries world over.

Today, Amul's range of products includes milk powders, milk, butter, ghee, cheese, dahi, yoghurt, buttermilk, chocolate, ice cream, cream, biscuits, shrikhand, paneer, gulab jamuns, flavoured milk, basundi among others, and the list is still growing. As a testimony to its

quality, Amul's sugar-free Pro-Biotic Ice-cream won The International Dairy Federation Marketing Award for 2007.

While the Sun has set for Kurien, the light he lit for Amul continues to burn bright, fuelled by the determination, passion and perseverance of every contributing character to this story.

Today, from Kashmir to Kanyakumari, from Gujarat to Arunachal Pradesh, Amul is a saviour for many little Asmas (*while this character here itself is fictional*) who dream of healthy and nutritious food. It is a delicacy for many that brightens up their day. Amul represents India's unique strength in cooperative movements and its deep-rooted competence in science and technology in shaping country's destiny and economy.

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THE STIRRING UP OF A

# MILK REVOLUTION



## PRIOR TO 1945



Farmers of Kaira depended on seasonal rains for livelihood, just like farmers elsewhere in the country. The milk produced from their cattle was sold at throwaway price, thanks to the middle men.

## 1946

In a meeting between Morarji Desai and the farmers of Kaira, it was resolved that milk producers' co-operative societies should be organized in each village of Kaira District to collect milk from their member-farmers.



## 1948

The Union began pasteurizing milk with just a handful of farmers in two village co-operative societies producing about 250 litres a day.

## 1956



A new dairy with the ability to process extra milk into products like butter and milk powder was opened.

## 1965

The National Dairy Development Board (NDDB) was established at Anand.



## 1974

IPCL started the production of India's first milk sachets with low density polyethelene (LDPE).

## 1945



The Bombay Milk Scheme was established where milk had to be transported for 427 km, from Anand to Bombay.

## DECEMBER 14, 1946

The Kaira District Co-operative Milk Producers' Union Limited, Anand was formally registered.



## 1953

The 'problem of plenty stuck' and the farmer-members had no regular market for the extra milk produced in winter.

## 1964

Amul produced India's first indigenous baby food from buffalo milk



## 1970

NDDB came out with the dairy development programme for India, popularly known as "Operation Flood" or "White Revolution".

Since then, India has transformed from a milk deficient nation into a milk sufficient one and is today, the largest milk producer in the world.

SOURCE: <http://www.amuldairy.com/index.php/about-us/history>



## A cut above the rest - The sparkling story of India's diamond processing industry

*By Nissy Nevil*

It was the 1970s. Two hostel roommates, Arvind Patel and Dhirajlal Kotadia were in the final year of their Diploma studies at Rajkot. Arvind Patel was pursuing Diploma in Electronics and Radio engineering. Dhirajlal Kotadia was pursuing Diploma in Electronics and Sound engineering. Though their areas of expertise were different, they had one thing in common –curiosity – and this led to endless discussions on a range of things.

After their final semesters, it was time to pack their bags and bid adieu to each other. Arvind Patel went on to become a biomedical and electronics engineer and was working at Indian Space Research Organisation (ISRO)'s Space Application Centre (SAC) at Ahmedabad. He was introduced to lasers at SAC, in a laser unit used for ceramic cutting and drilling, gifted by the United Nations. Dhirajlal Kotadia too was introduced to lasers at Electronic Corporation India Limited (ECIL) in Hyderabad during his industrial training. He completed his training and went to Chennai to start his own business.

Who knew, within few years they would script a new chapter in the country's future!

Surat, a small town in Gujarat, was famous for textiles, international trade<sup>1</sup> and diamond processing. The town was home to a large number of *Hira Karigars* (diamond cutters) who continued the profession of diamond cutting and polishing that started around the beginning of 13<sup>th</sup> or 14<sup>th</sup> century<sup>2</sup>. Meddling with primitive tools designed and engineered during the years between the First and the Second World Wars, the *Karigars* were struggling to make ends meet.

As Surat was emerging as a pivotal commercial hub, both Arvind Patel and Dhirajlal Kotadia relocated to Surat, albeit, independently. The two later formed a team to supply electronic

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<sup>1</sup>Surat was one of the business ports during the pre-British time: Parveen, S. (2014). Surat: As a major port-town of Gujarat and its trade history *IOSR Journal of Humanities and Social Science* 19(5):69-73. (<http://www.iosrjournals.org/iosr-jhss/papers/Vol19-issue5/Version-6/K019566973.pdf>)

<sup>2</sup><https://erstwhilejewelry.com/blogs/stories/history-of-diamond-cutting>

devices of industrial applications at Surat. This is when the duo spotted a sparkling opportunity, quite literally, that turned the fortunes of Surat and its *Karigars* and put Surat on the global map in the diamond cutting industry. And thus, began the story of how technology revolutionised the traditional diamond processing industry in India.

## Why cut a diamond?

Chemically, diamond is just a form of carbon. The fact that the carbon atoms are arranged in a particular way makes it the hardest substance ever known, and also the most expensive gem. It is this arrangement that is also responsible for the glitter and the sparkle that diamonds are famous for.

Every diamond has a unique story, and this unique story of what makes a diamond is its 'cut' and the way it is polished. A diamond is a crystal and it can be polished only in certain preferred crystallographic directions. The hardness of the diamond varies with crystallographic directions. This makes it one of the most difficult gem materials to facet<sup>3</sup>. A facet refers to one side of a many sided cut gem. Through the cutting process, a diamantaire or an expert in diamond cutting seeks to create facets on the diamond that returns maximum light by the process of total internal reflection. This reflected light together with the light bent at the surfaces gives the diamond its sparkle.

The cutting process begins with the arrival of the rough diamonds, which are first sorted and then examined for defects, impurities and inclusions<sup>4</sup>. They are then sent to a diamond expert or a marker, who evaluates every single uncut piece and evolves methods as to yield the maximum market value from the rough diamond. Depending on this examination, an expert plans the largest diamond with the highest clarity.

## Traditional diamond cutting

In the absence of advanced tools, the diamond processing industry was marked with intense labour and depended much on human expertise. For instance, the diamond expert had to examine every rough diamond that arrives and marks the precise cleaving locations on the rough diamond crystal with indelible ink to guide the cutting process. The marked diamond is then sent to cleaving and/or sawing process.

<sup>3</sup>Caspi A. (1997) Modern diamond cutting and polishing. *Gems & Gemology* 33(2):102-121.

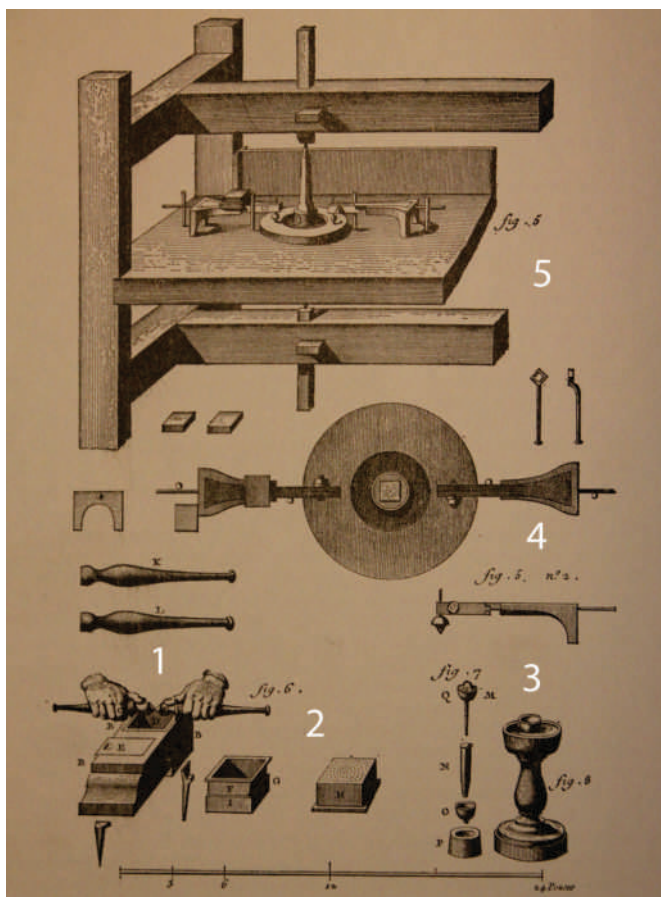
<sup>4</sup>Gaywala, R. (2015). Laser cutting transforms the diamond processing industry. *Industrial Laser Solutions for Manufacturing* 30(4).

During the cleaving process, the diamond was first glued onto a slot in a wooden rod with lacquer glue. Then, another polished diamond with a sharp edge was used to scratch on the marked locations of the rough diamond to form a groove. This process is called 'kerfing'. Next, a blunt blade was placed on the groove and tapped on with a small hammer, resulting in the diamond instantaneously cleaving and dividing into two. In the sawing process, a rough diamond was cut into two.

In either process, since the cutting involved manual labour, it randomly broke the diamond, resulting in huge losses in terms of market value for the diamond. The labour-intensive process yielded just 8-10 diamonds per day. The illustration given here shows the tools for diamond processing used in the 18<sup>th</sup> century<sup>5</sup>. With the advance of technology, diamond powder blades were introduced for sawing and cleaving, which greatly reduces the processing

time of the gem. After cutting and/or sawing, the diamonds receive a basic shape through a process called 'bruting'. In this process, a diamond was given a shape by rubbing it against another diamond that would either be rotating or kept in a static position.

In the final stage, facets are created on the diamond, in a process referred to as blocking, and are then sent for polishing.



*Eighteenth Century diamond working tools: 1. Bruting; 2. Container/sieve to collect diamond powder produced by bruting; 3. Dopping; 4. Wheel & Quill; 5. Polishing rig*

*(Image Credit: "File-Polishing Machine 1770". Via AJU [http://www.langantiques.com/university/File:File-Polishing\\_Machine\\_1770.jpg#mediaviewer/File:File-Polishing\\_Machine\\_1770.jpg](http://www.langantiques.com/university/File:File-Polishing_Machine_1770.jpg#mediaviewer/File:File-Polishing_Machine_1770.jpg))*

<sup>5</sup>[http://www.langantiques.com/university/A\\_History\\_Of\\_Diamond\\_Cutting](http://www.langantiques.com/university/A_History_Of_Diamond_Cutting)

## The diamond boom in Surat

Once famous for its textile industries and international trade, Surat began to register a growth of the diamond cutting industries from late 1950s. Diamonds were bought from trading centres in Antwerp in Belgium and Israel. Back then, the diamonds received in Surat were low-quality rough diamonds rejected from Israel, Belgium and other places. These diamond pieces were either difficult or commercially unviable to cut in these countries. With efficient and cheap labour in Surat, the units here got them cut and exported them back to the diamond merchandising countries. Gradually, the diamond processing industry in Surat started growing and the trade started shifting from Israel to India.

This shift in trend called for the *Karigars* in Surat to give up labour intensive processes and adopt new technology to satisfy the demand. But, technological advances in the diamond processing industry in India were scarce. This was the opportunity that Arvind Patel and Dhirajlal Kotadia were waiting to grab.

The duo's first successful contribution in introducing technology to Surat was, in fact, not related to diamond processing at all! They developed an electronic weft feeler for looms in the textile industry, which acted as an electronic 'eye'. The looms of that time were plagued by two issues with the equipment that affected the quality of the fabric, unless detected on time. One was when the yarn on the weft exhausted and the other was when the internecine stoppage of shutter of the loom moved from one side to the other. The newly developed weft feeler could sense both.

In addition, the weft feelers hitherto used had an auto lamp that guzzled power and required frequent replacement of the lamp. In their new weft feeler, Arvind Patel and Dhirajlal Kotadia replaced the lamp with a much more efficient and power saving infrared sensor, and eliminated the lamp altogether. This product became successful and is still widely used in the textile industries.

It was 1988. The success of the electronic weft feeler gave them the confidence to foray into the diamond industry, where technology infusion was needed to make the process of diamond cutting and polishing more efficient and economical.

In the 1970s, when high power laser equipment was being developed in the West, the Indian diamond industry was oblivious to this development. Industrial lasers were being used in Europe and USA for niche applications. One such application was the replacement of mechanical sawing of diamonds with lasers.<sup>6</sup> In this process, a focussed, high power beam

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<sup>6</sup>Caspi, A. (1997) Modern diamond cutting and polishing. *Gems & Gemology* 33(2):102-121.



from a YAG (Yttrium Aluminium Garnet) laser strikes the diamond placed on a computer-controlled sample holder that can move in horizontal and vertical directions. When the focussed laser beam strikes the diamond, it heats the spot to high temperatures, eventually vaporising it. As the diamond moves under the fixed laser beam, a slice is created. This process had many advantages. Lasers being focussed as high-power beams had certain advantages over mechanical and manual sawing methods. There is no mechanical contact between laser and diamond; hence the process does not generate any mechanical stress on diamond during cutting. Since the laser beam is not limited by preferred crystallographic directions, it could saw a rough diamond in any direction, thus resulting in greater accuracy, yield, ease in handling complex rough diamonds and minimal weight loss. Soon, lasers were also used for drilling diamonds, bleaching or dissolving dark inclusions<sup>7</sup> in the diamonds.<sup>8,9</sup>

Arvind Patel and Dhirajlal Kotadia had heard from various sources that the De Beers Company in South Africa, the largest diamond producer in the world, had started using laser machines to cut diamonds. The duo decided to procure a laser machine and try it in India. After a thorough search, they located a laser machine supplier in Switzerland.

Sceptics and cynics laughed and scorned at the idea of bringing a laser machine from abroad to India to cut diamonds. The import price of the laser machine was too high – about Rs. 60-70 lakhs at that time. But Arvind Patel and Dhirajlal Kotadia were determined, and they sought the help of a diamantaire friend who was already exporting diamonds, to procure their first laser machine. Once the laser unit arrived from Switzerland, they studied the machine, its working and mastered it. During the day, they used it to make grooves on the diamonds for their customers and during the night, they opened the entire machine to understand its components and figure out a way to reverse engineer it.

The machine consisted of a laser unit comprising of a laser source, beam delivery optics, power supply, cooling system and a CNC automation unit that worked by means of computers executing pre-programmed sequences of machine control commands. These machine control commands are usually written in G-code computer language, which is complicated. Since every rough diamond is unique in its size and shape, the laser-cutting machine had to be programmed with specific cutting requirements, which was very rigid and cumbersome. Even

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<sup>7</sup>Inclusions are dark visible spots in the diamond formed by the presence of graphite or sulphide minerals or other iron-containing mineral phases. Diamonds with these dark inclusions were not that highly value as those without them, their presence effected the clarity of diamond.

<sup>8</sup>[https://en.wikipedia.org/wiki/Laser\\_cutting](https://en.wikipedia.org/wiki/Laser_cutting)

<sup>9</sup>Overtone, T.W. and Shigley, J.E. (2008). A history of diamond treatments. *Gems & Gemology* 44(1):32-55.



writing a G-code snippet for each diamond required programming knowledge and was time-consuming.

That is when the duo got Rahul Gaywala on board. Rahul was a computer programmer and a chemistry graduate hailing from a family of goldsmiths. He had picked up mechanical skills involved in goldsmithery from his family, and had picked up electronics as a hobby. With the right set of skills in his pocket, he was soon entrusted with the responsibility of managing the computer software and integrating it.

Now, the core team consisted of Arvind Patel—the technical expert, Dhirajlal Kotadia – the entrepreneur and marketing expert and Rahul Gaywala—the software expert. Armed with the synergised skill and knowledge of technical advancement, the trio began their journey into the diamond processing industry.

### The first waves of technology

In diamond processing, whether manual or laser-based, the first step is to form a groove on the diamond, in a process known as kerfing. This marks the exact position where the diamond needs to be cut. This initial task was assigned to Rahul, who was to write a computer program that would come up with the appropriate size and shape of the groove, based on the size and properties of a rough diamond. Since diamonds varied in size and shape, Rahul wrote a collection of 5-6 programs to handle this. Thus, in a few days, he created the first laser processing software for diamond industry in India—a giant leap forward.

Now, with the introduction of the machine, 50 diamonds could be cut in just 10 minutes as compared to 8-10 diamonds that would be cut in a day without a machine. In order to have a better capacity, Dhirajlal Kotadia invented a simple mechanism to create a cassette full of diamonds and have them all grooved together. He used a plastic compass box with a top lead and 4 slots. A diamond was glued onto each slot and the laser beam was guided through each of them. This increased the pace of cutting and generated huge revenues with which they were able to repay all their debts within a year.

As laser kerfing started picking up, the trio realised some of the limitations of this machine. The first was that these machines were not designed for Indian conditions, especially for its weather and power fluctuations. A series of blackouts and power cuts, common during the 1980s, often caused the machine to break down. Repairing the machine was a daunting task. Either they had to pay for the airfare for an engineer to fly from Switzerland who would come when convenient, or take out the component, go to their headquarters, wait in a hotel for few

days and get it fixed. It was a frustrating situation. This set the stage for building a laser machine in India for India.

## **Building the empire of laser technology**

Convinced that developing an indigenous laser machine was the way forward, the trio started putting together the components needed to build the machine. They started sourcing whatever they could find within the country. They also started designing some parts themselves. As for whatever they could not make themselves or get in India, they took their diamond exporter friend's help to import those parts. Finally, in 1991, they built two laser machine units for diamond cutting, the first ever laser machines built in India for diamond cutting. This heralded a laser era in Indian diamond industry.

However, things did not change overnight. Initially, when the team, introduced the laser-cutting machine to the diamond cutters, they were not very receptive to it. They feared losing their source of livelihood. Soon their fears were allayed when they were educated by the team on operating the machine and its benefits. As the company grew, mechanical engineers, software engineers and electronic engineers from Surat and nearby cities were carefully handpicked to join the team.

Over time, the laser-based machines evolved and the laser beam became narrower and sharper. This resulted in reduced energy consumption and could now cut diamonds better, end-to-end. Lasers units were now employed for kerfing and sawing of diamonds. As the laser beam became narrower and finer, their tolerances became better. Better tolerances lead to super fine mechanical engineering elements supported by newer software algorithm. As tolerance was being developed, newer methods were developed and refined.

During the mid-90s, Sarine, an Israeli company, introduced machine planning of rough diamonds into the market. Here, the diamond rotated on a turntable, and the machine scans all the areas of a rough diamond and reconstructs a 3D model of the diamond. It then plans and prints instructions for manufacturing cut diamonds from the rough diamond. This process is more accurate and systematic than the one involving human decisions as it is guided by an algorithm and is not prone to human error.

This technology of planning involving algorithms for cutting rough diamonds was developed at the Sahajanand Technologies. Today, the conventional methods of planning and marking of diamonds is totally replaced by software-based vision and laser system units. With the success of these lasers, Arvind Patel went on to develop the first fibre laser for cutting applications.<sup>10</sup>

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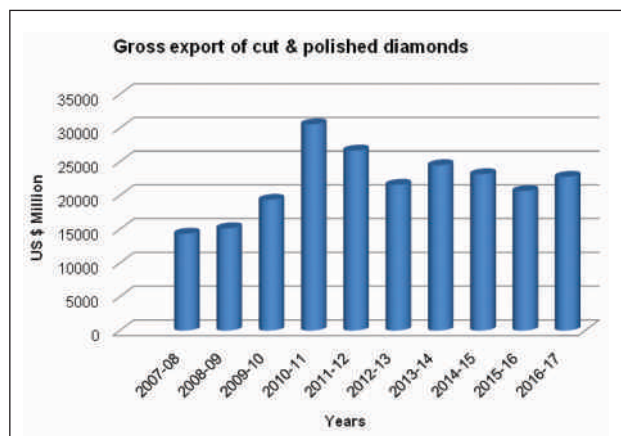
<sup>10</sup><http://www.sltl.com/diamond.html>

Considering his contribution in Indian Laser Industry, Government of Gujarat honoured Arvind Patel with 'Dr Vikram Sarabhai award for Young Scientists in the field of Industry' for the year 1997-98. He also has been awarded many national awards, one from Department of Science and Technology, Govt. of India. Arvind Patel credits his out-of-the-box thinking to the late scientist Prof. U.R. Rao at Community Science Centre, Ahmedabad who challenged him with practical mathematical puzzles in his school days. Dhirajlal Kotadia too has received many awards for his contribution and in 2017, he and his team created history by inventing world's first robot for automatic diamond processing, completely developed in India.

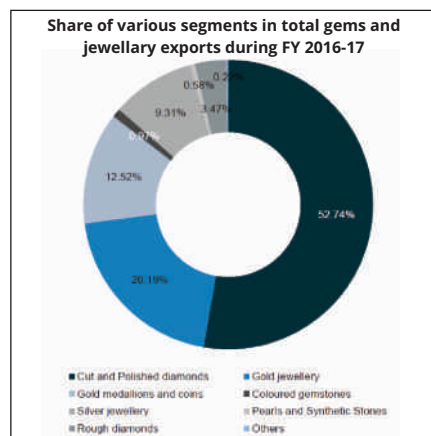
### Impact of mechanisation on diamond cutting

Hitherto, in the early days of diamond cutting industry in India, it was a small cottage industry that relied heavily on expertise and skill. About five to ten artisans used to work together in cottages without any formal training, and learnt the tricks of the trade through experience. The remunerations were low; they were paid based on the number of pieces of diamonds they worked on. Technology has now changed it all. Today, a single laser-based diamond cutting machine can cut about 600 to 900 diamonds per day.

India has now become the world's largest diamond cutting and polishing centre<sup>11</sup> largely due to adoption of the latest laser techniques in the early 1990s. It exports over 95% of its cut and



Data Source: <https://www.gjepc.org/statistics.php>



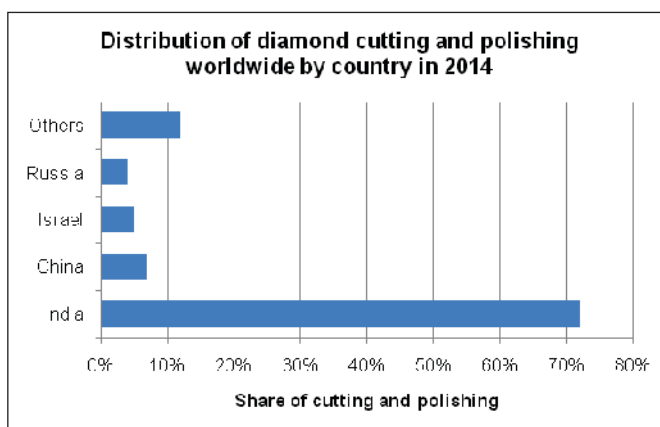
Data Source: [https://www.ibef.org/download/IBEF\\_Gems\\_and\\_Jewellery\\_September\\_2017.pdf](https://www.ibef.org/download/IBEF_Gems_and_Jewellery_September_2017.pdf)

<sup>11</sup><https://www.ibef.org/exports/gems-and-jewellery-export.aspx>

polished diamonds, accounting for 75% of the world's polished diamonds.<sup>12</sup> The Indian gems and jewellery sector contributes to about 6-7% of the Gross Domestic Product (GDP) of the country. The overall exports of gems and jewellery during April-December 2016 stood at Rs. 175, 879.24 crores (USD 26.28 billion), whereas exports of cut and polished diamonds stood at Rs. 113, 171.17 crores (USD 16. 91 billion). During April 2016 – March 2017 period, cut and polished diamonds registered a growth of 10.24%.

Cut and polished diamonds account for the highest share of 52.74% among the total gems and jewellery exports. The graph below shows the various segments in total gems and jewellery exports during the fiscal year 2016-17.

Today, there are more than 12,000 laser units operating in the diamond city of Surat. Prior to these technological innovations, family businesses and independent diamond cutters from Antwerp, New York and Israel ruled the diamond cutting and polishing business and Indian diamond merchants did not have any impact on the global market until the mid-1970s. With the expansion of lasers in the Indian diamond industry, Surat has now become the most important hub for diamond cutting in the world. While the largest and most valuable stones are still polished abroad, Antwerp has lost nearly 90% of its cutting jobs, and Israel 70% of its cutting jobs, to Surat.<sup>13</sup>



The impact and reach of science and technology has now transformed one of the sleeping towns of Gujarat into a world leader in the art of diamond processing. Further advancements in laser-based diamond processing industry are on the anvil to take Indian contributions to greater heights.

Data Source: <https://www.statista.com/statistics/588958/diamond-cutting-and-polishing-global-distribution/>

<sup>12</sup><https://www.ibef.org/industry/gems-jewellery-india.aspx>

<sup>13</sup>Richman, B.D. (2015). How community institutions create economic advantage: Jewish diamond merchants in New York? In *The Global Diamond Industry Economics and Development* Volume II Eds. Roman Grynberg, Letsema Mbayi, Springer.

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# The manual processing of Diamonds

## Careful examination of the diamond



Carefully examining the diamond for any obvious flaws

## Marking the diamond

The mark acts as an indicator for the final shape that the diamond will take



## Cleaving the diamond

This process divides the diamonds into two pieces roughly



## Sawing the diamond

This process consist of presciently dividing the diamond into two pieces



## Diamond burting

The diamond gets its rough shape through this process



## Polishing the diamond

The diamond is polished to get the final product







## A scarlet pouch endowed with life: Blood bag

By Kavita Tiwari

I was enjoying a quiet Sunday evening at home. It was hours before Moonrise, so I picked up the remote and settled back on the couch. I surfed the channels for a while and was about to call it a night when a scene from the movie *Amar Akbar Anthony* caught my eye. A car knocks down an old, blind woman, who sells flowers on the street. Three young men (take a wild guess as to who they are!) end up in a public hospital with the woman. When the doctor says she is weak and needs a blood transfusion, coincidentally, all three young men happen to share her blood group and are willing to donate.

The men lie down in beds placed parallel to each other, while the woman lies unconscious on a fourth bed at their feet. Then, in one of the film's most memorable visuals, a miraculous direct transfusion takes place – the blood begins to flow from their arms and into a common tube, from which it flows into the arm of the old lady. Later, the audience discovers (surprise, surprise) that she is none other than their mother!

I have watched the movie countless times, but never had the ludicrousness of the whole affair struck me so forcibly. The fact that the protagonists were linked through an implausible serial blood transfusion, where the mother ends up receiving blood transfusion from, wait for it – all three of her sons at the same time made me laugh and roll.

What's more, the old woman and the three siblings survived the 'mother' of all blood transfusions! Back in 1977, when the movie was released, the entire blood transfusion system in the country was on the verge of witnessing the single most influential innovation in blood banking – the development of the plastic blood-bag. If the director and screenwriter had got their facts right, the scene might have panned out something like this:

The blood, drawn from the veins of these three young men, would have been collected and stored in bags. These bags would have then been taken to the blood bank, which would have been exchanged for the blood that was needed to save their mother's life. Of course, that would have changed the course of the movie, quite literally.

The story presented here coalesces around the revolutionary phase of the blood transfusion system of the country. The blood bag is at the heart of the therapeutic services and each event is a plunge into its history and making. It is a story that gives a rich glimpse into the research competencies underlying scientific advances in the country. To uncover its inception in India, I went to the place where it all began – Sree Chitra Tirunal Institute for Medical Sciences, Thiruvananthapuram. A few memoirs of effort and research are unfolded in the present story.

### **Sree Chitra Tirunal Institute for Medical Sciences Technology**

(SCTIMST) is situated in Thiruvananthapuram, Kerala. It is one of the premier autonomous medical schools and an Institute of National Importance in India. It was founded by Chithira Thirunal Balarama Varma, the last ruling king of Travancore (and named after him), for the benefit of the people of Kerala at the Satelmond Palace, Poojapura. The Biomedical Technology Wing (BMT) followed soon, again a gift by the Maharani Sethu Lakshmi Bayi.

Established in 1974, the institute employs clinicians, scientists, and engineers devoted to biomedical research and developing technologies in healthcare, especially cardiovascular and neurological diseases. SCTIMST has a university status and offers postdoctoral, doctoral and postgraduate courses in medical specialties, public health, nursing, basic sciences and health care technology. Prof. M.S. Valiathan headed SCTIMST from 1974 to 1994.

### **A nation's medical need**

In the 1970s, blood transfusion services in India did not use the state-of-the-art technology, like disposable blood bags. Hospitals and blood banks depended entirely on glass bottles, despite their obvious disadvantages –hygiene concerns, high breakage rates, exorbitant cleaning costs, and problems in centrifuging. India needed to get rid of using out-dated blood transfusion services. In a bid to improve the blood transfusion system of the country, the Government of India proposed a National Blood Transfusion Service (NBTS), to be modelled on a similar service in the UK.

A British consultant, who was invited by NBTS, suggested that the re-usable glass bottles could be replaced with disposable plastic blood bags. The latter were considered safer for the collection and storage of blood and blood components the world over.

Even today, the advantages provided by the bags remain unmatched. Apart from being light, these plastic blood bags are tear-proof (i.e., they cannot be torn without scissors or cutters), compact, and easier to handle, and have lower rates of bacterial contamination. Separation of different blood components is possible and cleaning processes aren't needed any more since they are disposed-off after single use. These small wonder pouches have brought about the much-needed transformation of the blood transfusion services across the world. In addition, a global increase in the incidence of blood related disorders promoted the growth of disposable plastic blood bags market.

“A steadily growing market for medical devices in the post-World War II years had, in fact, created a multimillion dollar industry abroad and an estimate of India's imports had placed their annual price tag at Rs. 400 to 500 million in the early 1970s”– reads an excerpt from one of the articles written by Prof. M.S. Valiathan, Founding Director of Sree Chitra Tirunal Institute of Medical Sciences and Technology (SCTIMST), Thiruvananthapuram, highlighting the growing demand of biomedical devices in India.



*The Biomedical Technology Wing (BMT Wing) located at the Satelmond Palace at Poojappura, Thiruvananthapuram where the first blood bag was developed. (Photo Courtesy: Dr. Kavita Tiwari)*

At the time of independence, India was an utterly poor economy with widespread illiteracy and horrific poverty. For a huge country like India, the changeover from glass bottles to plastic blood bags would necessitate the import of the entire requirements, resulting in a huge drain on its limited foreign exchange reserves. The only alternative left was to develop and manufacture blood-bags in the country. Fortunately, rather than spending such whooping amounts on imports, the country chose to invest in the challenging realms of innovations and inventions – a path of delving in our own strengths through indigenisation.

## **Biomaterial and bio-devices research in India**

Post-independence, India started taking aggressive and confident strides in its road to scientific development. Escalating non-communicable diseases and a sharp increase in incidences of infectious diseases in the country hastened the ever-increasing role of S&T in medicine. An illiterate and poverty-stricken population further contributed to the medical liabilities of the government. Initially, science and technology (S&T) made baby steps, but gradually took on ambitious projects. One such institution was SCTIMST, which grew rapidly over the years in investigations that sparked off scientific interest, and increased in social relevance and industrial potential.

The oxygenators performed the task of a heart, pumping oxygen into blood. It consisted of two poly-vinyl chlorides (PVC) sheets welded together in such a manner that they provided, in sequence, a bubble chimney wherein oxygen was bubbled through a rising column of venous blood, a defoaming chamber and an arterial column from which blood was pumped back to the patient.

At this critical juncture, the institute shifted focus on biomaterials and medical devices which had failed to attract the attention of planners and national research bodies. Prof. Valiathan, having established a first-rate cardiac surgery unit at SCTIMST, got back to his love for medical devices and biomaterials. For a hospital specializing in cardiology and neurology, the passage to accomplish the development of biomaterials and medical devices was full of highs and lows. The first few projects were nothing less than a herculean task for the team at SCTIMST.

Prof. Valiathan's vision kick started the technology development program at SCTIMST. It was during the first phase of an ambitious program that a handful of curious scientists took up the development of an oxygenator, a disposable device used in open-heart surgeries. Executed in close collaboration between different departments of SCTIMST, the oxygenator project was funded by the Department of Science and Technology (DST), Government of India. A team of

scientists at SCTIMST worked relentlessly to ensure that every detail of the oxygenator was perfect and set the gold standard.

Who knew that oxygenators would one day become a trendsetter for the development of a more complex system (blood bags) in the country?

Dr. Satyendra Nath Pal led the team developing the oxygenator. A graduate in Polymer Technology from the University Department of Chemical Technology (UDCT, now named Institute of Chemical Technology or ICT), Mumbai, Dr. Pal took his first job at SCTIMST and set up his own laboratory to develop disposable medical devices. Apart from two engineers, Dr. S.N. Pal and A.V. Ramani, the team included a polymer chemist Dr. V. Kalliyana Krishnan. Dr. Jayaprakash, Shri C.V. Muraleedharan and Shri P.R. Hari were also part of the team.

While the consensus presented a relatively basic roadmap for developing an oxygenator, problems were bountiful. The biggest challenge was finding the right raw material for making oxygenators. "PVC was our first and only choice", says Dr. Pal on choosing a suitable biomaterial. PVC is inert, durable, and resistant to chemicals. It is impervious to heat/cold, abrasions and kinking, and possesses the ability to withstand steam sterilization. PVC comes at a low cost and could be heat-sealed. For the development of oxygenators, PVC formulations had to be converted into sheets. During the initial phase of development, SCTIMST had no machines/equipment to convert PVC formulations into useable sheets. Commercially available PVC sheets posed bio safety concerns.

Dr. Pal and his team used the PVC sheets, which were specially calendared for them by Bhor Industries, a Mumbai based company. Calendaring is a finishing process in which polymers, paper, plastics, rubber, or textiles are pressed into sheets and smoothed, glazed, polished, or given an embossed surface.

"The difficulties in the development of the oxygenator were aggravated by our concern that no industry would care to produce the oxygenator since its demand was unlikely to exceed three to four thousand a year", wrote Prof. Valiathan in an article in the journal *Current Science*, talking about the numerous problems the team faced. Nevertheless, there was a general optimism among the team members that these problems could be remedied. "The institute was very new at that time and we didn't have any facilities to begin with. We were all very young but hopeful when we first started working on the oxygenator project", reflects Dr. Pal.

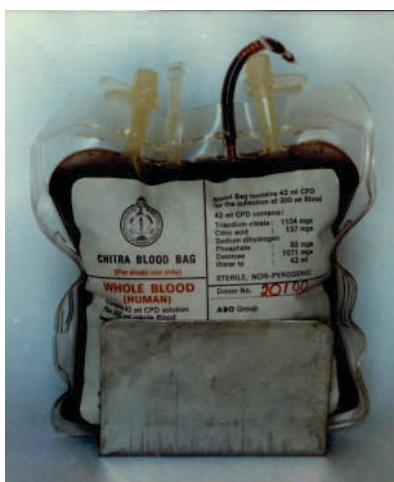
### **PVC and its derivatives: Promising polymers for blood bags**

The success of oxygenator stemmed the idea of using the same PVC sheets to make blood bags. Statistical data from the Union Health Ministry indicated that the proposed national

blood transfusion service would need two million bags a year, which reflected a possibility of creating a nascent market for biomaterials.

Initial samples of the designed blood bags were made from the PVC sheets used for making oxygenators. But the samples cracked during centrifugation – one of the crucial tests for selecting a candidate bag, which involves rotation at a very high speed. The team realized the necessity to develop a new PVC-based polymer, which could withstand centrifugation. Other requirement for a new PVC-derivative was properties that would allow release of minimal quantities of phthalate, a hazardous substance produced during storage of blood.

Dr. Pal and team eventually developed a novel PVC formulation for making blood bags. But it took the team nearly three years to produce a prototype blood bag, which fulfilled the standards recommended by the Department of Health and Social Security (DHSS), UK. Dr. Kalliyana Krishnan, from the blood bag team at the SCTIMST, recalled how they worked all night after the demand for the Chitra blood bags soared high in the market. “The approach,” wrote Prof. Valiathan, “demonstrated that medical technology could be developed quite successfully within the country by creating a joint institutional framework for medical science and technology.”<sup>3</sup>



*(Left) The Chitra blood bag: First 'blood bag-single' developed at SCTIMST*

*(Right) First 'blood bag-double' developed at SCTIMST.*

*(Photo Courtesy: Dr. S.N. Pal)*



SCTIMST developed the technology needed for manufacturing blood bags in conformity with the international standards. Their first blood bag was successful in all *in-vitro* trials, experimental use in a few hospitals, and scrutiny by the Ethics Committee at SCTIMST.

“Development of blood bags has gone through different levels of difficulties. First, the concept, then the material, and then the product itself—everything was new to both the parties; Penpol and SCTIMST. Ultimately, here was a product which was of immediate need to the user”, asserts Dr. Kalliyana Krishnan on their success. He further adds, “It was an import subsidiary; the prices fell by an order of one-fifth to one-tenth. What were once sold for 1500 rupees and more, became 100 or 150 rupees. It is even cheaper now.”

Apart from paving the way for the subsequent development of PVC bags for blood storage and the fabrication of titanium housing for a heart valve model- which connected the blood bag to the patient, the DST project helped in building a team of competent scientists and engineers at SCTIMST. The biomedical engineers came from the Indian Institutes of Technology (IITs) and other engineering colleges and the inputs from personnel trained abroad were minimal. Thereafter, the institute encountered a favourable climate for intensifying the technological effort in producing innovative biomaterials for future endeavours. No one could ever think that apart from the blood bags being 'Purn Swadeshi' – (completely indigenous), the team behind the endeavour was also equally indigenously groomed.

Dr. Krishna believes that the real success of the SCTIMST team lay in meeting the need of the hour and creating a well-designed product, which could be immediately used. As the supply met demand, prices fell and the blood bags became affordable and user-friendly.

### Challenges faced during development of the Chitra Blood Bags

1. Development of a non-toxic formulation: Separate non-toxic formulations had to be developed for sheeting, tubing, injection moulding – which shaped the blood bags, and ports- which connected the blood bags to the patient. It took nearly 70 batches of polymer batch preparations (4 Kg) to finally arrive at the correct non-toxic formulations. At the time, working without the guidance of established parameters and guidelines for the blood bag industry was no mean task.
2. Non-availability of proper processing equipment: There were no processing machines to prepare sheets of PVC on a large scale and the team had to resort to outside agencies. However, these industrial units were preparing commercial grade PVC sheeting. So, the team at SCTIMST could not get clean transparent sheeting in the initial stages and thus had to discard many batches of sheets.

3. Optimization of sterilization process was the biggest hurdle in making the blood bag. Conventional autoclaving resulted in bags bursting up. Ambient gamma radiation resulted in oxidization and browning, a phenomenon named caramelization, of anticoagulants. Ethylene oxide sterilization resulted in PVC retaining the gas, thus turning toxic. The number of bags getting damaged during production was overwhelming. However, this problem led to standardization of a new technique of sterilization that is currently being practiced by the industry—sterilization using compensatory air pressure.
4. Quality control: Training of the scientific personnel and other human resource for processing of blood bag system sapped both time and energy. Often, the bags lost their sterility due to these issues. Educating people and spreading awareness about blood bag usage was another effort by the team to curb quality and usage related complaints.

“We had to dig information about what all should be the safety parameters before setting our foot further as there were no standards, no guidelines for us”, points out Dr. Pal as he mentions about the challenges faced by the team in developing blood bags. He further retorts by telling us, “The only thing available was a submission from someone in the UK who was trying to develop a blood bag during 1978-79”.

“The innovation we did was aimed at cutting the cost of the final product and improving the design of the bag for better applicability and quicker acceptance compared to what was available at that time”, emphasizes Dr. Pal.

## **Blood Bags foray into the markets**

Rome was not built in a day. So weren't the blood bags; success didn't come easy. It was in 1984 that the team at SCTIMST could finally freeze a prototype blood bag. Due to the slow progress of the project, many were unaware of the development of blood bags. Hence, despite efforts to persuade several companies in the public and private sectors, the team could not find a manufacturer.

Two years later, a science reporter covered one of the symposia at the SCTIMST and wrote about the blood bags. The article elicited a few enquiries from entrepreneurs. As Prof. Valiathan and team had no prior experience in technology transfer for commercial use, Dr. Varadarajan, then Secretary of DST, arranged for a meeting with two consultants from the Indian Petrochemical Corporation Limited (IPCL) to assist the SCTIMST team in the task.

Captivated by a local newspaper article on blood bag technology, a young bureaucrat embarked on an entrepreneurial journey that led to pioneering success in manufacturing indigenously developed biomedical devices in the country – Mr. C. Balagopal. Balagopal served as an IAS officer and later left the service to set up a company to manufacture blood bags in India. Balagopal had no industrial experience or background, but his drive, knowledge, and tenacity to succeed made an impression on everyone. He was particularly enthused about pioneering the manufacture of a life-saving device because of its potential for making a social contribution.



*A man with many hats: Mr. C. Balagopal*  
(Photo Credit: Mr. Balagopal's Twitter account)

After serving in the Indian Administrative Service (IAS, 1977 batch) as an officer from the Manipur cadre, Balagopal shifted gears to join National Research Development Corporation (NRDC), which was on the lookout for entrepreneurs to transfer workable, indigenously developed technologies for creating new business ventures. The technology for manufacturing blood bags developed by SCTIMST was one such project.



*A donor's blood being collected in a  
blood bag developed at SCTIMST*  
(Photo Courtesy: Dr. S.N. Pal)

Beckoned by the challenges of an 'untested' new technology and a new product, Mr. Balagopal resigned from his service and plunged into the uncertain but exciting world of entrepreneurship for manufacturing a high technology medical device. Based on the technology transferred to him by SCTIMST, he started a venture called 'Peninsula Polymers (Private) Limited' or Penpol, which was incorporated in 1983 with its registered office in

Hyderabad. It was fortunate for the company that Prof. Sivaraj Ramaseshan, former Director of Indian Institute of Science (IISc) and the Editor of the journal *Current Science* agreed to be Penpol's Founding Chairman. Penpol was the sole manufacturer of blood transfusion bags in India at that time.

In February 1984, after signing the technology transfer agreement with the NRDC, Penpol shifted to Trivandrum. The relocation aimed to facilitate better collaboration with SCTIMST for developing the blood bags commercially as well as for setting up a manufacturing plant. Hence, NRDC not only assigned the license to Penpol, but also promoted the company with the Kerala State Industrial Development Corporation (KSIDC). NRDC also provided equity assistance of up to 25% of the total equity for setting up a plant.

NRDC licensed the blood bag production technology to Penpol for Rs. 2 lakhs and 3% royalty on sales; to Hindustan Latex, Trivandrum, for Rs. 12 lakhs and 3% royalty; and to Trade East, Indonesia, for \$685,000 (Rs. 2 crores) and 3% royalty.<sup>1</sup> Each of the licensees catered to India's requirement of affordably priced blood bags. Blood bags were also exported to countries like UK, USA, Germany, Netherlands, Kenya, and Bangladesh. The technology has been earning valuable foreign exchange since then.

Who knew that a basic process developed by SCTIMST could produce a leading market player like Penpol! Dr. Kalliyana Krishnan comments, "Now it is a much-matured technology. Today if you want to manufacture blood bags, you don't have to go to any labs or need any technology documents. You simply approach the machine manufacturer. So, the technology transfer is in the machine. It is that easy now. So, this is the kind of transformation that has gone into making the blood bags after more than 33 years of technology transfer. 45 million bags make Trivandrum the blood bag capital and for that we should thank SCTIMST and the Chitra Blood Bag team."

## Challenges in technology transfer

One of the biggest challenges for any new technological venture is to master the know-how involved in the manufacture and servicing of the product. The transfer of technology posed its own problems, but the involvement of SCTIMST in setting up the Penpol factory in Trivandrum was quite helpful. Preparing a detailed project report, training the Penpol technicians during the pilot production of blood bags in the SCTIMST laboratories, deputing engineers for the selection and installation of equipment, and many other things were done in a truly cooperative spirit as neither side could afford the risk of a failure.

### The look of a blood bag

In its unused state, a blood bag looks like a thin transparent deflated vacuum suction bag, with a tube sticking out of the top. It is a deceptively simple product but has a highly sophisticated manufacturing process. Blood bags are quite complex. Blood bags consist of a plastic bag, connecting tubes, outlet ports, special flow regulating valves, filters, safety features, sampling ports, needles, and so on.

Despite all the help from SCTIMST, Penpol too faced several difficulties, as there were no readymade documented procedures available for the manufacture of blood bags. An array of problems such as defective quality of raw material, problems of dust and particulate matter in the anticoagulant, leaks, poor label quality and unsatisfactory quality of needles bogged Penpol initially. Of course, there were a few international companies, which manufactured blood bags, but their technology was proprietary. There were hardly any literature or consultancy services available on the process. Many of the problems faced by Penpol were unique and unprecedented.

In hindsight, Mr. Balagopal must have felt that it was a huge mistake to jump into the venture without having a pilot plant in operation. Many of the technological problems experienced by Penpol arose from an initial perception that the blood bags were a simple product to make. The unique design of the blood bags enables safe collection, separation (into components like red blood cells, plasma, platelets and so on), preservation, and transfusion of blood. Large-scale manufacturing of these components was an arduous process.

Hoping to find solutions to the problems from the technology providers, Mr. Balagopal approached SCTIMST, but they were unable to help as the project team that developed the indigenous blood bag technology had been disbanded and its members reassigned to other projects. It was then that Penpol decided to do independent 'research' and master each step in the manufacturing process on its own.

Scaling threw up numerous challenges; many were of a very serious nature without ready-made solutions. Neither the technology suppliers nor the agencies could help Penpol overcome them. A process technology that works in a beaker can't be taken and dropped directly into a 200-gallon tank. An effective lab scale process technology requires an experienced engineering specialist to successfully scale-up a pilot or production plant.

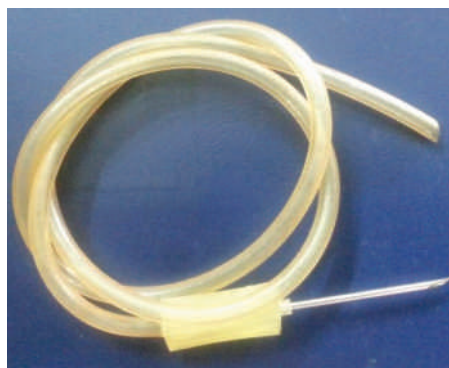
While Penpol was struggling to stay afloat, one person who played a significant role in scaling up the technology was Dr. C.S.B. Nair, a name that notably and unfortunately has missed mention. Using the bench scale data provided by SCTIMST, Dr. Nair, a passionate and experienced chemist, used his scientific knowledge to successfully scale-up the technology. Nair single-handedly managed the entire R&D operations at Penpol and achieved the scale up through his proprietary industrial process design that was both time-efficient and cost-effective.

### Dr. C.S.B. Nair

Dr. Nair obtained his B.Sc., M.Sc., and Ph.D. degrees from University of Kerala, Thiruvananthapuram. He started his career as a Research Assistant at the Central Research Institute of the University of Kerala in 1946. He then joined the Central Fuel Research Institute, Dhanbad, Bihar and worked there as a scientist for 27 years. Subsequently, he joined the Fertilizers and Chemicals (FACT), Travancore Ltd. as Head, R&D. After his retirement in 1984, Dr. Nair joined the newly formed M/s Peninsula Polymers Ltd., as Head, R&D. At Penpol, he was entrusted with a unique task of developing the technology for manufacturing blood bags. After successful development of the technology, he continues to work as a consultant for the company (now Terumo Penpol Ltd).

“When we started, everything was new – the blood bags, polymer, company, employer, employees – everything”, recalls Dr. Nair, now a 91-year-old young man, musing on his life experiences. With a twinkle in his eyes, he adds, “That’s a very good thing – when you have a blank sheet, you can draw whatever you want to. But it is not as simple as it looks.”

In 1985, after considerable deliberations with Dr. Nair, Mr. Balagopal decided to assess the SCTIMST process on a small scale. The trial production went off without a hitch even though there were



*Needle attachments used by Penpol Ltd for their first batch of blood bags*

*(Photo Courtesy: Dr. Kavita Tiwari)*



knowledge gaps and problem areas that had to be addressed. However, Penpol could make 30 bags per day with the limited facilities available. By the end of 1987, a full-scale plant was built at Puliarakonam, a suburb of Trivandrum, around Uma Studios- a film studio which belonged to the famous Malayalam film actor, Sri Madhu.

## Unavailability of raw materials

Although Penpol was equipped with an annual installed capacity of 2 million blood bags, its initial production in July 1987 was on a very small scale. The main constraint for large-scale production was that there were no suppliers of medical grade PVC (plastic granules) in India. The special additive for making the non-toxic PVC compound was being imported at that time. The high import duties levied on the product put it beyond Penpol's reach. The only viable alternative was to make quality in-house material. The R&D team at Penpol took it upon themselves and succeeded in making high quality plastic granules in sufficient quantities to meet their manufacturing requirements.

## Taming the greenish overlay on labels

Penpol started commercially manufacturing blood bags from 19<sup>th</sup> March 1987. Having solved the raw material problem, the company started producing and marketing their bloodbags. In the meantime, financial contingencies and mounting pressures from their new marketing set-up forced Penpol to send out thousands of blood bags across the country. While Penpol managed to tackle several pressing concerns, they were soon overwhelmed by an unanticipated problem- fungal growth on blood bag labels. Customers reported discoloration of labels on the blood bags from some batches. Almost each one of the blood bags, created

with great attention and care, developed dirty looking greenish coatings on the labels. In addition, there was water accumulation within the outer cover of blood bags and even more serious, a change in composition of the anticoagulant solution.



*Different types of needles being used since 1985 at the Penpol factory, Trivandrum*

(Photo Courtesy: Dr. Kavita Tiwari)

Mr. Balagopal took an almost suicidal, but ultimately wise decision to recall every infected bag from the market and destroy it – a decision that caused terrific monetary loss to the fledgling company. The problems were traced to deficiencies in the packaging and sterilization systems. In what was another bold move, Mr. Balagopal decided that in the absence of technical help from external people, Penpol should solve their problems by their own R&D efforts. Production was withheld for a year. In the meantime, R&D efforts at the company succeeded in overcoming the difficulties. With such trust reposed in him, and knowing that it was a question of survival for Penpol, Dr. Nair rallied with enthusiasm. Soon his efforts began to pay off. The nature of fungal growth was clearly identified and eliminated by improved processing steps. The problem of packaging and sterilization were solved by the introduction of new methods.

### **R&D efforts at Penpol by Dr. Nair**

Penpol decided to make changes in the blood bags for use as containers for intravenous solutions such as Saline, Dextrose and Ringer Lactate, which was very successful. In due course, Dr. Nair could standardize the manufacturing operations to meet the Indian Standards for IV solutions. He also developed an improved design for urine bags, which went into production and was well accepted by the market.

Detailed R&D studies of the blood bag system and changes during sterilization by autoclaving indicated that the water accumulated in the space between the blood bags and outer cover was derived from two sources:

1. One was from the autoclave itself. Steam penetrated from the autoclave condensed within the outer cover. The material it was made up of had to be reconsidered and redesigned.
2. As much as 60% of accumulated water came from the anticoagulant solution within the blood bags. Dr. Nair devised a novel procedure to remove the water, which condensed in the outer cover of the blood bag without causing deleterious changes to the blood bag system. Such problems were ultimately solved by the selection of appropriate packing system and selection of safe procedures for the sterilization cycle. All such processes are novel and are protected by Indian patents. With these innovations, M/S. Peninsula Polymers Ltd. decided to start the manufacturing operations in May 1988.

Dr. Nair's numerous contributions to the commercialization of the technology for blood bags at Peninsula Polymers Ltd., won the Department of Scientific and Industrial Research (DSIR) National Award for R&D in the year 1995.

Dr. Nair recalls that some Germans once asked him how he managed to build world-class technology to produce blood bags in a remote village like Puliyarakonam. It was remarkable that Penpol succeeded without any external support, braving criticism from international players. With people like Dr. Nair, who even at the age of 91 has deep intellectual and physical agility, it is no wonder that success was at the doorstep. "Even today, I'm trying to improve the packaging for reducing the cost. Let's see if the company allows me to do that", quips Dr. Nair.

The company eventually created a system that fully complied with the Good Manufacturing Practice (GMP) of the pharmaceutical industry. The strict adherence to a customer-centric quality policy has held Penpol in good stead even when domestic competition increased with Hindustan Latex Limited (a public-sector company) entering the market as another licensee to the SCTIMST-NRDC technology.

## Export and global reach initiatives

Penpol rolled out its first exports of 40,000 blood-bags to the Philippines in 1989. The next export was to the Union of Soviet Socialist Republics (USSR), whose health ministry approved the quality of Penpol's blood-bags. Soon, there were business partnerships established in the Middle East, the UK, Italy, Germany, and Greece.

The Government of India recognized Penpol's successes and the company received both the Top Exporters Award and the National R&D Award in 1995. Its exposure to foreign markets helped in making a vigorous comeback at home. The domestic sales of blood bags increased substantially. Penpol could wipe out the accumulated loss and persuade Industrial Development Bank of India (IDBI) to invest for its capacity expansion.

## Economic advantages

The commercial success of biomaterial based medical devices brought in monetary returns and social benefits to the country. Apart from direct savings in foreign exchange, the lower price of the competitive indigenous products has, in every instance, helped to keep down the price, by avoiding the cost of their imported counterparts—something that led to an increased participation and investment by other industries from the R&D stage.

The global disposable plastic blood bags market was estimated to be valued at USD 200 million as of 2016, while the current global consumption of disposable plastic blood bags stands at around 220 million units per year. (2)

“We started with the vision of developing an indigenous life-saving device, but we never knew that one day, the same blood bag would be exported to 80 countries. We never started with that thought”, murmurs Dr. Pal on his innovation.

Scientists and engineers at the SCTIMST and Penpol are proud of their research competencies in developing innovative indigenous biomedical marvels like plastic blood bags and heart valves. They have not only proven their research expertise towards manufacturing biomedical polymers, but also at making them safe for use in medical applications.



*The team members of the blood bag project; Photo taken at SCTIMST on July 18, 2017. From left to right: Shri C.V. Muraleedharan, Dr. V. Kalliyana Krishnan, Dr. S.N. Pal (fourth from left) and Dr. C.S.B. Nair from Penpol (extreme right) (Photo Courtesy: Dr. Kavita Tiwari)*

The initial scientific training received in Indian educational institutes has had a great influence on the development of these technologies in the country. It is the convergence of research abilities and integrated organizational efforts and inputs that have made the blood bag story such a success. Working with constraints and challenges at every step, each of the players added value to creating a progressive indigenization plan and ensuring its implementation. Prof. Ramaseshan, Founding Chairman of Penpol, aptly nicknamed the entire process as “intelligent copying” many years ago, as many of the ideas on materials used and production techniques were borrowed from developed countries, but also had to be tailored to a regional context!

The importance of the blood bag in health care cannot be overstated: one unit of blood can save up to 3 lives. “At the time when we started, it was just a research challenge. But now,

whenever I visit any hospital and see a blood bag, imagine the kind of satisfaction one derives from it,” exclaims Dr. Pal.

While blood bags also had their imitators over the years, India remains a proud franchise of owing one of the largest blood bags producing company in the world. Blood bag production by two industrial units (Penpol and Hindustan Latex Ltd.) alone accounts for 45 million bags per year. Penpol proudly claims of having over 38% of the global blood bag production.

The fascinating story of blood bags is a saga of how relentless scientific pursuit and enterprise have given millions a new lease of life—a pioneering example of a home-grown R&D initiative finding commercial success. Today, improvising research proficiencies in the country continues to be crucial for innovation in the science and technology domain.

## Acknowledgements

Author would like to acknowledge Prof. M.S. Valiathan for providing the initial details about the blood bag story; Dr. S.N. Pal and Dr. V. Kalliyana Krishnan for their first-hand account as the main inventors of the blood bags; and Mr. C. Balagopal for the visit to Penpol factory at Puliyarakonam, Thiruvananthapuram. Help and support from Shri Muraleedharan, Dr. Roy Joseph and Dr. Shiny of SCTIMST; and Mr. Mani and Dr. C.S.B. Nair of Penpol is gratefully acknowledged.

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# PENPOL

## THE COMPANY'S HISTORY

**1983**

Peninsula Polymers (Penpol) Pvt Ltd., a brainchild of former IAS officer C. Balagopal was set up.



**1987**

Penpol, in partnership with SCTIMST, started production of blood bags in its factory in Thiruvananthapuram, Kerala, on 26<sup>th</sup> March 1987, with TTK Pharma as its sole sales agent.



**1987**

Faced with manufacturing defects, the company had to close its operations in October 1987. The R&D team went all out to understand problems and find solutions. The major problems were change in the composition of anticoagulant, accumulation of water within the protective cover of blood bags and fungal growth.

**1988**

Having tackled the above challenges, Penpol restarted their manufacturing operations.



**1989**

Penpol sent out its first export shipment and expanded its R&D division.

**1996**

Started manufacturing equipment for blood transfusion and allied equipment.



**1999**

Penpol entered a joint venture with the multi-billion-dollar Terumo Corporation of Japan, and changed its name to Terumo Penpol (TPL). The company won the National Award from the Government of India for successful development of indigenous technology.



**2001**

TPL began the export of equipment for blood transfusion and allied equipment.







## CIBA – Riding on the waves of India's aquaculture

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*By Kavita Tiwari*

A visit to Arumai's paddy farm in Ambal in the Nagapattinam district, about 315 km away from Chennai in Tamil Nadu, is different from the rest. Apart from the lush green paddy crop, one can also find an unusual crop – prawns! Yes, tiny crustaceans that is a delicacy in many cuisines.

A first-generation paddy farmer-fisherman in his late forties, Arumai owns a couple of hectares of land to sustain his ten-member family. Until 1997, the production from the paddy farm was too little to meet the needs of his family. A chance meeting with a staff member at the Krishi Vigyan Kendra (KVK), Nagapattinam, left Arumai with an idea that would change his fortunes forever, or so he thought.

The KVK staff suggested co-culturing shrimp and prawns along with paddy, since growing paddy would require stagnant water in the fields. The idea of the income from selling shrimps and prawns feeding into his family income appealed to Arumai. Though initially hesitant about putting his hands on something he was totally new to, Arumai decided to pursue it anyway and became the first farmer in his village to start 'brackish water prawn farming'.

### **The seeds of prawn and shrimp farming**

Growing fish in rice fields is almost as old as the practice of rice or paddy. It is believed that fish culture in rice fields, also called 'paddy-cum-fish culture' was introduced into South-East Asia from India about 1500 years ago. Today, South-East Asia is the region with the best-developed technologies for fish farming.

Whenever water stagnates within bunds as needed for paddy, wild fish in the irrigation water and nearby tanks and pools enter the paddy fields. They grow and thrive in these waters until the paddy is harvested and the land is cleared. While early fish production in rice fields was based on capture rather than culture, production of shrimps and prawns was not. The integration of both finfish and shellfish (shrimps and prawns) with paddy in the fields has



*Paddy fields with  
brackish water can be  
used for prawn farming*

*(Photo Credit: Creative  
Commons)*

gained ground in the country since the last few decades. Prawns are mainly grown in brackish water regions along the Indian coastline in paddy fields. Till a few years ago, fishermen in India involved themselves in traditional marine fishing. In the 1970s, fishermen started concentrating on catching prawns and shrimps due to the high profits they would reap, thanks to the booming exports. Brackish water prawn farming started in a big way only during 1991-94 especially in the coastal districts of Andhra Pradesh and Tamil Nadu.

That is when Arumai also ventured into prawn and shrimp farming. The harvests were good and his income multiplied. Shrimps and prawns were now grown regularly as a 'cash crop' all year round, along with paddy. Alas, Arumai's happiness was short lived. In April 1999, a lethal viral infection called the white spot syndrome virus (WSSV) was reported in several farms across the states of Tamil Nadu, Andhra Pradesh, and Kerala, causing severe damage to shrimp culture in the country. Like other farmers, Arumai's farm was also affected and resulted in a decline in the shrimp production. Farmers suffered huge individual losses coupled with a decline in global market prices for shrimp.

Shrimps, infected with this deadly disease died within 3-10 days under farming conditions. First reported in China in 1991-92, the infection spread rapidly throughout the world causing huge economic losses to the global aquaculture industry. A report from the Department of Fish Processing Technology, Fisheries College and Research Institute, Tamil Nadu, estimated that 3,00,000 metric tons of shrimp was lost to this lethal virus during the last few years. Thus, the WSSV infection ate up the economy in a huge way. This is the story how few scientists working silently provided solutions to overcome this problem and revive Indian aquaculture.



*White spots seen in shrimp infected with WSSV*  
(Photo Courtesy: CIBA)

## The winds of change for Indian aquaculture

Aquaculture, also known as fish farming, refers to the breeding, rearing, and harvesting fish, crustaceans (like prawns and shrimps), molluscs (like mussels), aquatic plants, algae, and other aquatic organisms in ponds, rivers, lakes, and the ocean. Many families in rural India depend on aquaculture for their livelihood. It also plays a vital role in the socio-economic development of the country, providing income, employment, and the potential for export.

Today, fishing in India is already a major industry in all its coastal states, employing over 14 million people. Shrimp farming is a major activity pursued in brackish water. India has exported 11,34,948 ton of seafood worth an all time high of USD 5.78 billion (₹ 37, 870.90 crores) in 2016-17<sup>1</sup>.

Realizing the potential this activity could have on the economy, the Indian Council of Agricultural Research (ICAR) established many institutes to facilitate research and development in this direction.

Central Institute of Brackishwater Aquaculture (CIBA) was one such institute established in 1987, with a mandate to develop environmentally sustainable, economically viable, and socially acceptable aquaculture technologies. The organization played a major role in assisting small farmers in optimizing the finfish and shrimp farming by providing them with modern technologies. These steps have helped Indian aquaculture record an annual export revenue of ₹ 20,000 crores, apart from domestic consumption. In addition, CIBA also offers courses and research facilities for students, farmers, and entrepreneurs by regularly conducting farmers' meet, trainings, exhibitions, workshops and brainstorming sessions.

<sup>1</sup> <http://pib.nic.in/newsite/PrintRelease.aspx?relid=164454>



*Exotic shrimps are the major item of export from the country*

*(Photo Credit: CIBA)*

Dr. Jithendran, a senior scientist at the Aquatic Animal Health and Environment Division (AAHED) at CIBA, explains the role of aquaculture in shaping India's future. "Post-independence, India's population was burgeoning and food was scarce owing to famines. Insufficient food production led to starvation and deaths. That is when sustainable use of our vast water resources was thought of as a realistic solution to this problem. Eventually, fisheries together with agriculture, were recognized as one of the two most important sectors of the economy by the Indian government", he says.

For a country like India that is endowed with a long coastline of 8,085 km, ample land and diverse marine and freshwater aquatic life, aquaculture seems to be a natural choice. Our seas and rivers have many species of crustaceans, fish, molluscs, seaweeds that grow in various parts of the country. "The Indian government realized that there is enough potential to feed not just the population of the country, but also to export the aquaculture products. Soon, the government of India directly implemented a few projects with major thrust on fisheries development and promotion of aquaculture in the country. While growth of capture fisheries production had stagnated during the last two-three decades, aquaculture offered a vast scope of expansion", explains Dr. Jithendran.

However, shrimp farming on a commercial scale started gaining roots only after 1988-89. "Scientific shrimp cultivation took off as a pilot project at Nellore, in Andhra Pradesh, with funds from the Department of Biotechnology, Government of India. The Andhra Pradesh Shrimp Seed Production, Supply, and Research Centre (TASPARC)', along with DBT funds,



injected great impetus and interest in shrimp farming in India. An economic boom ensued, as the area under commercial farming increased substantially with a remarkable growth rate", explains Dr. Jithendran talking about the background of shrimp farming in India.

*CIBA has always empowered poor farmers by not only helping them with innovative products, but also imparting training through workshops and field outreach activities. News related to one such training in a national newspaper.*

(Photo Credit: [http://www.ciba.res.in/images/photo\\_gallery/Paperclip/CIBA%20News.jpg](http://www.ciba.res.in/images/photo_gallery/Paperclip/CIBA%20News.jpg))

4 TIMES CITY

\* THE TIMES OF INDIA, CHENNAI  
WEDNESDAY, JUNE 26, 2017

## SEEDS OF FISH FARMING SOWN IN ADYAR CREEK

Five Families Chosen  
By CIBA To Rear Fish In  
Restored Water Body

Opplip@timesgroup.com

**F**our decades ago the Adyar Creek, famed with fish, drawing birds from far-off shores for its fish. Today efforts are on to grow fish, albeit in cages, in the now restored but ecologically fragile water body.

Central Institute of Brackishwater Aquaculture (CIBA) has set up cages to help local fishermen harvest three species of fish. CIBA director K. K. Vijayan told TOI that after the creek was cleaned by Chennai River Restoration Trust, it was decided to help local fishermen by setting up cages in a portion of the water body. "Initially the species of sea bass, pearl spot and milkfish were released into the cages. We provided the feed for the fish. But only milkfish survived in the cages," said Vijayan. "Poor tidal movement could have affected the survival of the other two species we believe," he said.

For its pilot project, near Srivilliputhur after the creek was restored, CIBA has adapted the family farming mode. Since its launch in February, CIBA has trained 10 people from five families to feed the fish and monitor their growth.

Srivilliputhur resident TSP Ravi, one of the beneficiaries of project, said sand from the river had to be cleared regularly for the tidal movement to be favourable for fish culture. "A good tidal movement will help the fish grow," he said.

Since February, twice - once in two months - fish samples from the cages were collected and sent to Central Institute of Fisheries Technology for quality checks. This was necessary because the eastern side of the creek, a dumping ground for those living in the slum houses, is highly polluted. The laboratory results have been positive so far.

Ravi said a milkfish could be harvested in six months and a fish weighing 1kg would fetch ₹130, which the beneficiaries can share among themselves. "CIBA has given us a good livelihood option which will provide an alternative income in the future," Ravi said.

Vijayan said fishermen involved in the project need not work full time. "This is an ancillary activity. They have to visit the cages twice a day for feeding. They can attend to their daily businesses after that," he said.

By August-end, CIBA is hoping for a rich harvest and the fishermen good earnings. Vijayan said if the breeding of milkfish in the creek is successful and sustainable, more such cage-culturing can be taken up.

NEW LEASE  
OF LIFE



**LONG SURVIVOR:** Of the three species released in the cages (below), only milkfish survived.

### THE BLUEPRINT

> Three species of brackish water fish - sea bass, milkfish and pearl spot - will be reared in cages.

> Five cages have been sunk in the creek in a 100sqm area.

> First ever caged fish culture in the Adyar creek and estuary.

### THE TEAM

> A total of 10 people from five families selected by Central Institute of Brackishwater Aquaculture (CIBA) involved in project.

> They have been trained with cage installation, cage maintenance, feeding and postlarval sampling.

### THEIR CHANCES

> Water samples from six locations of the creek have been collected by CIBA.

> Collected water has been tested before fish were released in cages.

> Key soil and water parameters studied over period of 10 days showed the site was suitable for rearing specific varieties of fish.

### MARKET RATES (per kg)

SEA BASS ₹250 MILKFISH ₹150 PEARL SPOT ₹150

## Where old threats loom large

Times News Network

**C**lose to 400 crore may have been spent to restore the Adyar creek and estuary to its original glory by the Chennai River Restoration Trust (CRRT), but months of plans and perhaps an overlooking the ecosystem again.

A state government official said the Tamil Nadu Slum Clearance Board had built tenements to house those living in the slums. More than 50 blocks were built but around these tenements encroachments have cropped up.

A Srivilliputhur resident said more than 3,000 makeshift



houses had come up in and around the tenements. Waste water from these illegal structures drains into the creek polluting it, he said.

Ravi, another resident, said sewer from the illegal settlements must be routed to the pumping sta-

tion near Foreshore Estate bus terminus. "If this sewage pollution levels in the creek will come down and basins to restoration," he said. A senior official from the Slum Clearance Board said so far there was no plan to demolish the makeshift buildings along the Adyar creek. When contacted, a CRRT source said the Slum Clearance Board was organising awareness programmes in the slums on their behalf, advising people against dumping waste in the creek. "But with regard to the encroachments near the slum tenements, the government has to take a decision. It is not our mandate," the source said.

## The attack of the pathogens

While the shrimp industry started to grow and thrive, there was a lurking trouble – diseases. The period around 1995 gave a major jolt to the shrimp industry in India. Like Arumai, many farmers were left in the lurch after severe outbreaks of fatal shrimp diseases left them with no yield. The eggs that were available for sowing were also infected and the industry soon collapsed and turned into a loss-making venture. Exports fell too and caused a serious dent to the economy.

"Around 1995-96, viral outbreaks began to occur in shrimp farms, the likes of which hadn't been seen before", recalls Dr. Jithendran. "From then on, microbial diseases have been a major problem for aquaculture worldwide", he adds.

Shrimps, like us, suffer from a wide variety of diseases caused viruses, bacteria, fungi, and certain parasites. Various shrimp pathogens such as WSSV and lately, *Enterocytozoon hepatopenaei* (EHP) have caused havoc in entire Asia, including India, disrupting the shrimp production. In addition, the fact that most of the farmers were new to commercial scale shrimp farming, their ignorance of good aquaculture practices, and lack of suitable infrastructure led to a host of problems in this sector.

So what really made matters worse? “Diseases may have spread with infected broodstock (breeding fish). Another reason could have been the traditional aquaculture methods practiced across the country that do not allow much environmental and water quality controls. Majority of the farmer-fishermen in the country are largely unorganized, scattered, and poorly educated. They mostly opt for traditional methods for operating their farms, and do not have access to technological innovations or scientific applications”, explains Dr. Jithendran.

Tackling shrimp infections is a challenge, as they cannot be treated effectively in a pond. The saying 'prevention is better than cure' goes well here. Practicing good farm management, acquiring information on various kinds of diseases and their prevention procedures becomes crucial. If detected early, many diseases can indeed be prevented from reaching epidemic proportions. “Early pathogen detection became crucial to prevent the disease from spreading. Accurate and specific diagnosis is extremely important to achieve bio-security in shrimp hatcheries and farms”, says Dr. Jithendran.

In addition, all shrimp species cultivated in India are highly susceptible to microbial diseases, and many have wiped out several shrimp farms. One such widely known outbreak is that of WSSV during 1994-95, which caused a huge financial loss of ₹ 250-300 billion across the country. Prof. Karunasagar and his team first detected the disease in Indian shrimps in the year 1997<sup>2</sup>. In 1999, a team at CIBA showed for the first time that shrimps and crabs caught in the wild are also hosts for WSSV<sup>3</sup>.

To exacerbate the problem, there were limited therapeutic options available back to control these viral diseases. Hence, farmers were asked to take preventive measures like efficient pond management practices, use of proper feed, selection of good quality seeds, reduction of

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<sup>2</sup> Karunasagar, I., Otta, S.K. and Karunasagar, I. (1997). Histopathological and bacteriological study of white spot syndrome of *Penaeus monodon* along west coast of India. *Aquaculture* 153:9-13.

<sup>3</sup> Rajendran K.V., Vijayan, K.K., Santiago, T.C., Krol, R.M. (1999). Experimental host range and histopathology of white spot syndrome virus (WSSV) infection in shrimp, prawns, crabs and lobsters from India. *Journal of Fish Diseases* 22:183-191.



possible carriers, avoidance of introduction of contaminated water into the pond and disinfection of all equipment and utensils.

## CIBA's role in reviving India's aquaculture

Since its establishment, disease monitoring in brackish water aquaculture has been a major activity of CIBA. The innovative technologies developed by CIBA and its surveillance programs have resulted in the identification of lethal viral diseases in shrimps.

The development of an indigenous PCR-based (Polymerase Chain Reaction) technique, in the late 1990s, to detect WSSV viruses in shrimps at different stages of its growth has been a game changer for many farmers like Arumai. The biggest hurdle these farmers faced was to ascertain that the seeds and the broodstock used to produce them were disease free. So how could they ensure this? That is when the scientists at CIBA came with the idea of developing a simple, cost effective detection kit for farmers using the PCR based technique.

The other challenge that farmers faced, in spite of having their seeds tested in laboratories for diseases, was in trusting the lab results. "Usually, farmers give seeds to three to four laboratories for testing, mostly private ones. At times laboratories provide contradictory results leading to confusion among farmers. The fishermen, based on the results provided by these laboratories, take important decisions. So, it was important to standardize and validate test protocols for the results to be consistent and accurate", explains Dr. Jithendran. The idea of kits addressed this problem too.

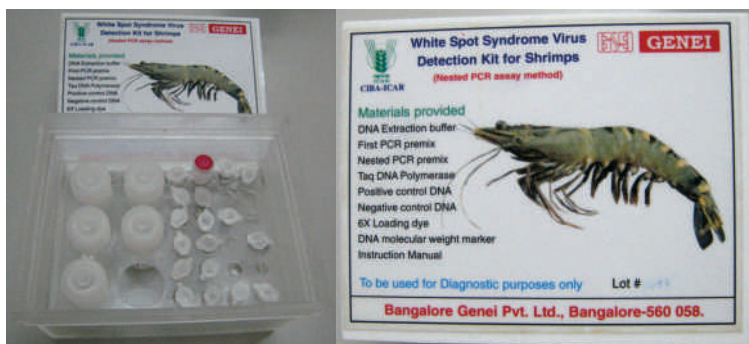
"Consequently, a nested PCR kit was indigenously developed and commercialized in 2002 by a Bangalore based company - M/s Bangalore Genei Pvt. Ltd. This kit is highly economical. Like all infectious organisms, WSSV is continuously evolving since it was first discovered. To meet this challenge, our team subsequently developed an advanced version of the same kit. In 2017, this advanced kit was licensed to a Chennai- based company called M/s Aura Biotechnologies Pvt. Ltd.", shares Dr. Jithendran.

The WSSV detection kit is the first such indigenous kit to offer a cost-effective solution to shrimp farmers to help control the WSSV infection. It made the detection process of a viral pathogen as simple as pushing a button. Later, PCR was used as a tool for detection of various other pathogens in shrimps and prawns.

"CIBA was instrumental in harmonizing these PCR tests among the laboratories to sustain the phenomenal growth of brackish water aquaculture and neutralize the threat of diseases", says a proud Dr. Jithendran.

## PCR-based detection

Polymerase Chain Reaction (PCR) is a molecular biological method for amplifying (creating multiple copies of) DNA without using a living organism. PCR is used to amplify a short, well-defined part of a DNA strand. This can be a single gene, or just a part of a gene. As opposed to living organisms, the PCR process can copy only short DNA fragments. During PCR, the DNA may be amplified several million times their original concentration. PCR-based tests are also extremely sensitive and much faster than the conventional diagnostic tests. PCR is commonly used in medical and biological research laboratories for a variety of tasks, such as the detection of diseases, the identification of genetic fingerprints, the cloning of genes, and paternity testing.



*First nested PCR Kit developed by CIBA that was commercialized by M/s Bangalore Genei Pvt. Ltd., Bangalore in 2002*

*(Photo Courtesy: Dr. K.P. Jithendran)*

A big push in CIBA's research activities came in 2002 with a MPEDA-NACA (Marine Products Export Development Authority – Network of Aquaculture Centres in Asia-Pacific) project, assisted by the Food and Agricultural Organization (FAO), to support shrimp farmers in disease control and coastal management. This enabled the development of many technologies for disease detection and management. Now, with such kits, farmers could ensure that their seeds were disease free and hence, they were promised of a good yield.

The techniques developed by the team at CIBA have applications beyond shrimps and prawns! They have now been used in diagnostic laboratories for monitoring health, to identify infections in environmental reservoirs and to detect the presence of pathogens in quarantined animals. Through several projects sponsored by Department of Biotechnology (DBT), CIBA has developed several products, and transferred its technology to different companies for commercialization.

“A research venture that first started for developing technologies to detect viral diseases in shrimp grew leaps and bounds. We knew that such technologies are going to be waves of the

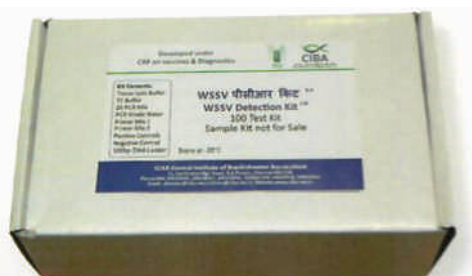
future, and we are determined to strengthen our position in global aquaculture sector. We began looking for alternative ways to spin off our indigenously developed diversified technologies at decent prices”, recalls Dr. Jithendran.

The other important direction for CIBA is to ensure that reliable disease detection facilities are accessible by all farmers in the country. According to a CIBA report, only 40-60% of PCR laboratories function reliably. To address this, it has now launched a nation-wide drive to accredit the laboratories that do PCR tests on aquatic animals.

In the process of accreditation, CIBA, being the national referral laboratory for brackish water aquatic animal diseases, regularly carries out studies to assess the quality of PCR screening done at these laboratories. In the next step, CIBA physically verifies laboratories and then conducts another round of quality assessment before giving the certification. This exercise would help maintain a healthy shrimp seed quality in the country and ensure sustainable shrimp farming. In addition, CIBA wants to create a pool of accredited labs to enable small farmers to get reliable PCR testing services.

“Our aim is to service the small-scale aquaculture sector of the country and provide technical support to poor farmers. We also work to empower and build the capacity of small-scale farmers to produce quality shrimps in a more profitable manner”, says Dr. Jithendran.

Technology cost, which was once a barrier for many farmers and laboratories, is now no more a concern. “The declining costs of using technologies over the years due to innovations of CIBA, and the resulting benefits, have made PCR techniques a big hit”, says Dr. Jithendran. Today, shrimp farmers, small and large, use only PCR-tested seeds for stocking. Private laboratories are now successfully providing cost-effective PCR detection services to the entire shrimp farming industry. In India, currently more than 300 laboratories are providing PCR services for the shrimp sector – mainly the screening of seeds and broodstock. “Hence a lot of scope exists for small fishermen/entrepreneurs to venture into this field of activity”, he adds.



*Advanced version of the WSSV kit  
licensed to M/s Aura Biotechnologies  
Pvt. Ltd., Chennai  
(Photo Courtesy: CIBA)*

Recently, researchers at CIBA have designed compact kits similar to the pregnancy test kits available at the pharmacy, for detecting other shrimp diseases. Using these kits, even unskilled farmers can easily diagnose shrimp disease outbreaks in their farms. The strips are relatively cheap and quick. Other methods comparable to PCR and RT-PCR are now readily available or are being developed for single, dual or multiple pathogen detection.



*Muttukadu experimental station of  
ICAR-CIBA, Chennai  
(Photo Courtesy: CIBA)*



*EHP detection kit developed by CIBA  
(Photo Courtesy: Dr. K.P. Jithendran)*

## Beating challenges – One at a time

Today, indigenously developed scientific technologies have not only revolutionized the Indian shrimp farming sector, but has also provided huge economic benefits to the farmers, and in turn added to the country's economic growth. Farmers now reap higher profits, incur lower production costs, and produce quality shrimps without using any hazardous chemicals. But, making this happen was not easy! The accomplishments of CIBA and its scientists did not come without challenges.

Back then when CIBA started out to solve the hurdles faced by shrimp farmers in the country, resources were scarce and so was time. “To complete all projects on time and on budget was something incredible that we all have been doing now for so many years”, says Dr. Jithendran adding – “We faced numerous challenges - lack of basic infrastructure being the foremost. You would be surprised if I were to tell you that we never even had a PCR machine at CIBA when we first started working on the project. There were absolutely no resources!”

The fact that farmers trusted in indigenously developed technologies, braced it rapidly and used these cutting-edge technologies at the grass root level, is a testimony to the efforts of

dedicated, capable people like Dr. Jithendran and others. Their focus on developing cost effective, reliable, in-house products without depending on foreign skills or technologies, to solve a range of problems existing in the Indian context is commendable indeed.

So what drove these scientists to excel in spite of the challenges? "I feel that to succeed, one must first believe that he/she can. We believed in our capabilities and so we did it. As a good team, we worked day and night. I believe this was crucial in the alignment of experienced manpower and proven scientific talent for the R&D feat that we foresaw. I don't know how we did it all, but I think it was meant to be. The past is behind us, there's no looking back now," says Dr. Jithendran with joy and pride.

So the next time you are savouring a plate of shrimp curry or prawn pickles, it is time you recollect the enormous efforts of farmers like Arumai and scientists like Dr. Jithendran, who help you put them on your plate. The success of shrimp aquaculture industry in India is a classic example where scientific innovations and state-of-the-art technology have transformed millions of lives and empowered poor.

*Note: While Arumai is a fictional character, he represents large number of farmers who have benefited from scientific solutions to the problems of Indian aquaculture.*

## Acknowledgements

Author would like to thank Dr. K.P. Jithendran at CIBA for his patience, time and help.

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## 1 WSSV NESTED PCR KIT <sup>2.0</sup>

Early detection of WSSV in shrimps

## 2 EHP NESTED PCR KIT

Detection of *Enterocytozoon hepatopenaei* of cultivated shrimps.

## 3 'β NOVA' VNN DIAGNOSTIC KIT

RT-nested PCR kit for the early diagnosis of VNN.

## 4 LUMI <sup>PHAGE</sup>

A safe and effective technology using bacteriophages for biocontrol of luminescent bacterial disease in shrimp hatcheries.

## 5 SHRIMP LARVI <sup>PLUS</sup>

Low cost alternate for expensive imported larval feeds.

## 6 VANAMI <sup>PLUS</sup>

Purpose: Cost effective indigenous feed using locally available ingredients. This is a boon for small and medium shrimp farmers.

## 7 CIBASTIM - SHRIMP GROWTH PROMOTER

Selected microbial based product for application along with the feed as top dressing developed using cost effective indigenous technology.

## 8 CIBAMOX

A unique formulation for management of ammonia, with safe and natural microbial consortia selected through arduous R&D efforts. It was developed using indigenous microbes isolated from local brackish water environments so that it works best in Indian shrimp farming systems. Low cost alternate for expensive imported larval feeds.

## 9 POLY <sup>PLUS</sup>

Suitable low cost feed for poly culture developed using locally available ingredients having a long shelf life.

## 10 INDIGENOUS SHRIMP FEED TECHNOLOGY

Feed is a critical component of shrimp farming that not only determines the growth performance of the shrimp, but is also a key factor related to cost of shrimp production and sustainability. No single public or private entity in India had the technology to manufacture pelleted sinking feed for shrimps. To reduce import-dependence for feeds, CIBA developed and tested an indigenous feed manufacturing technology as a pioneer in the country.

## 11 MODULAR SYSTEM BASED SEED PRODUCTION

Innovative low cost model for backyard breeding and seed production of pearl spot.

## 12 BREEDING, SEED PRODUCTION AND FARMING OF MILKFISH

A comprehensive innovative package for captive breeding and seed production of MilkFish.

## 13 SEED PRODUCTION AND FARMING TECHNOLOGY OF ASIAN SEABASS

Seabass is a fast growing, high value carnivorous fish ideal for farming in wide range of salinities. While its standard table size is 500g to 3 Kg, it can grow to a size of 2 meters long and 60 kg weight. CIBA made a breakthrough in equating its biological and culture potential.

## 14 INTERVENTION ON INTRODUCTION AND FARMING OF VANNAMEI SHRIMP IN INDIA (AN INNOVATION DEVELOPED USING INFORMATION TECHNOLOGY)

Before the year 2008, shrimp aquaculture was centered on the black tiger prawn as the single most important species. When the aquaculture sector was struggling with the devastating WSSV disease which caused huge economic losses, farmers wanted to import specific-pathogen free (SPF) vannamei species from the western world. CIBA framed the import guidelines and BMP's. Risk and impact analysis was jointly done with ICAR-NBFGR. CIBA provided technical support for creating the quarantine facility and developed FAQ's with answers and an android based mobile app (Vanami Shrimp app) for *Penaeus vannamei* farming knowledge transfer.





## Provocation, precedence and innovation: How Shantha Biotechnics shaped India's biotechnology future

*By Adita Joshi*

This story of Shantha Biotechnics, the first company to establish recombinant DNA technology in India, highlights the scientific prowess of Indian scientists, entrepreneurs and their spirit of nationalism.

But how did it all start? What transformed India, a country that was once considered home to many diseases, turn the tables by becoming a leading producer of many lifesaving vaccinations? It was emotions – a lot of them and thus goes the story.

In the beginning of 1993, K.I. Varaprasad Reddy, a man in his early forties was treading the corridors of Udyog Bhawan (Ministry of Commerce) which stood tall in Lutyen's Delhi. He was trying to trace his application seeking a licence to manufacture a recombinant DNA vaccine. After much effort, his application was traced to the Department of Engineering amidst other submissions on engineering and machine tools!

Surprised and bewildered, Varaprasad later understood what had transpired. The application whose title read 'Genetically engineered hepatitis B vaccine', obviously ended with the engineering department! Those days, when there was not much difference between 'engineering' and 'genetic engineering' for the common man, the staff thought that the proposal was on an engineering product.

It was those times when regulatory roadmaps for production and testing of recombinant DNA technology based innovations were gradually evolving. Pharmacopoeia—a list containing names, formulas and methods to prepare medicines—was defined for regular generic drugs and chemical compounds, but was alien to products of recombinant DNA technology.

### Recombinant DNA

Recombinant DNA is a name given to the DNA molecules that are formed by bringing together genetic material from multiple sources in a laboratory. Recombinant DNA is possible because DNA molecules from all organisms have the same chemical structure.

## A game changing provocation

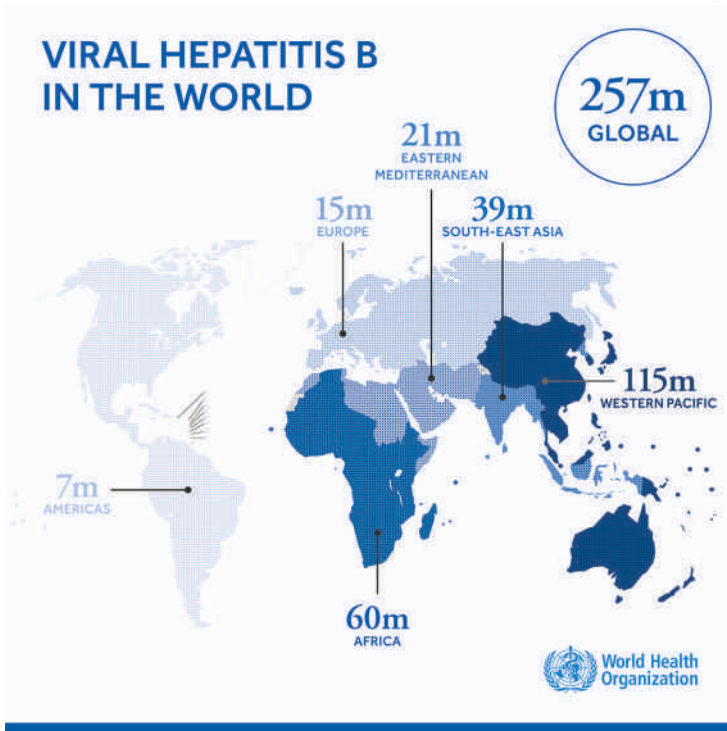
Interestingly, it was provocation that made K.I. Varaprasad Reddy, an electronics engineer from Hyderabad, wander the corridors of Delhi. You might wonder what an electronics engineer, working at that time as a defence scientist, had to do with DNA and vaccines. Once, Varaprasad was visiting his cousin, Dr. Varada Reddy, who worked at the Environmental Protection Agency (EPA) in Cincinnati, USA. While on his way to attend a conference organised by World Health Organisation (WHO) in Geneva, Varada asked Varaprasad to casually accompany him. Little did he know that the visit would turn out to be life changing!

### **The problem: Economics and market monopoly**

Hepatitis B vaccine was sold at a rate of Rs. 750-850 per dose with one or two multinational companies commanding the market monopoly. Preventive vaccination required a total of three mandatory doses. In those days, spending Rs. 2,250-2,550 per member was unthinkable for most Indian families. For a family of four, probably the vaccination cost was either more than or equal to the monthly earnings. People chose to either die or preferred medical intervention after contracting the disease rather than getting vaccinated. The choice of getting the shot was limited only to the rich who could afford private healthcare services. The 'Geneva experience' had enthused in Varaprasad, a ferocious desire to make an affordable hepatitis B vaccine that could reach masses and children of India.

During a discussion on a talk titled "Impact of immunization", Varaprasad heard about hepatitis B for the first time and instantly got curious about it. On returning from the conference, he contacted local doctors in the USA to know more about hepatitis B. Varaprasad gathered the important facts: hepatitis B was life threatening; preventive vaccination was available, but was a costly affair and developing countries were hopelessly dependent on multinational companies for procurement of the hepatitis B vaccine. In India, it was a neglected disease in spite of the fact that it contributed to a considerable number of deaths.

Motivated, shamed and provoked about India's inability to have a vaccine against the disease, Varaprasad wanted to change it all and make the preventive vaccine affordable to everyone in the country. That is when his tryst with biotechnology began.



**WHO World Hepatitis Report Infographic:** An estimated 257 million people are living with hepatitis B virus infection (defined as hepatitis B surface antigen positive)

(Source: <http://www.who.int/news-events/global-hepatitis-report-2017-infographic/en/>)

## Raising support and money for India's first vaccine start-up

At a time when there was no 'start-up' frenzy like today, and venture capitalists were few, raising support for the big idea was not easy. Especially for an engineer trying to enter an unknown terrain of vaccine making, it was an effort no less than a space mission. Varaprasad knew that his idea needed the scaffold of scientific sharpness, else it would never see the light of the day.

On his return to India, he contacted the founder of Dr. Reddy's Laboratory and INTAS pharmaceuticals to undertake the project, but he was disappointed. Both the companies refused to take up the project as it was strongly believed then that such technological ambition is risky from a business angle. "People found it difficult to believe that the vaccine could be easily produced in India. They wanted to help, but doing risky business was not their cup of tea", recalls Dr. Varaprasad.

Resolved to pursue his big idea and produce a vaccine, Varaprasad did not deter. With no scientific partners coming onboard, he decided to try and obtain the technology on his own. He contacted Varada in the US to set up a meeting with Genentech, the developers of hepatitis B vaccine. The agenda was to obtain the technology transfer from the Smithkline Beecham Biologicals, only major manufacturer of hepatitis B vaccine. The meeting was unfruitful and left Varaprasad with judgemental comments. The representatives from Genentech, which had developed and transferred the technology to Smithkline Beecham, opined that *India, as a country can not afford the technology*. For Varaprasad, this experience culminated in a clear writing on the wall - development of indigenous technology.

If one knows the final destination, half the journey is done. Varaprasad was determined to have the final vaccine product in hand. Together with Varada, he organized a get together of expatriate Indian scientists, friends and acquaintances working in the US to inform them about the need for hepatitis B vaccine. A few scientists offered commitment to train people from India, if Varaprasad could nucleate a small team of scientists back home. The 'big idea' and Varaprasad's steadfastness diluted the drawback of his lack of biotechnology background. A few of his classmates and his cousin offered monetary support of Rs.1.22 crore. By selling a part of his paternal property, Varaprasad added another 68 lakh to reach Rs 1.9 crores – his initial capital for the new vaccine start up.

## Early sprouts at Osmania

With the necessary funding in hand, Varaprasad now started scouting for the technology and scientific acumen needed for realising his big idea. He started to look for collaborations with scientists and molecular biologists in Hyderabad. Having worked previously with Defence Electronics Research Laboratories (DERL), and Andhra Pradesh Industrial Development Corporation (APIDC), Varaprasad had experienced the potential and calibre of Indian science.

Dr. Malla Reddy, the Vice Chancellor of Osmania University was an acquaintance and agreed to provide a room in the University's microbiology department. The only condition was to refurbish the room which was in a poor condition. It costed about 5 lakh rupees for Varaprasad to renovate the dilapidated room to a laboratory. With this, the earliest sprouts of Shantha had come alive. Varaprasad was joined by Dr. Gita Sharma, a full time faculty at the microbiology department of Osmania University. Dr. Gita had earlier worked at the University of Rochester, New York, on interferons - proteins of the immune system. For Varaprasad, Gita was a dictionary that helped him build his vocabulary of recombinant DNA technology. She helped him write a proposal on the hepatitis B vaccine and parallelly started to work on interferons. Shantha Biotech was thus born, and the R&D centre started functioning in that small lab at Osmania in 1993.

*Dr. Gita Sharma and  
K. Varaprasad Reddy in a  
discussion during the early days  
of Shantha Biotechnics*

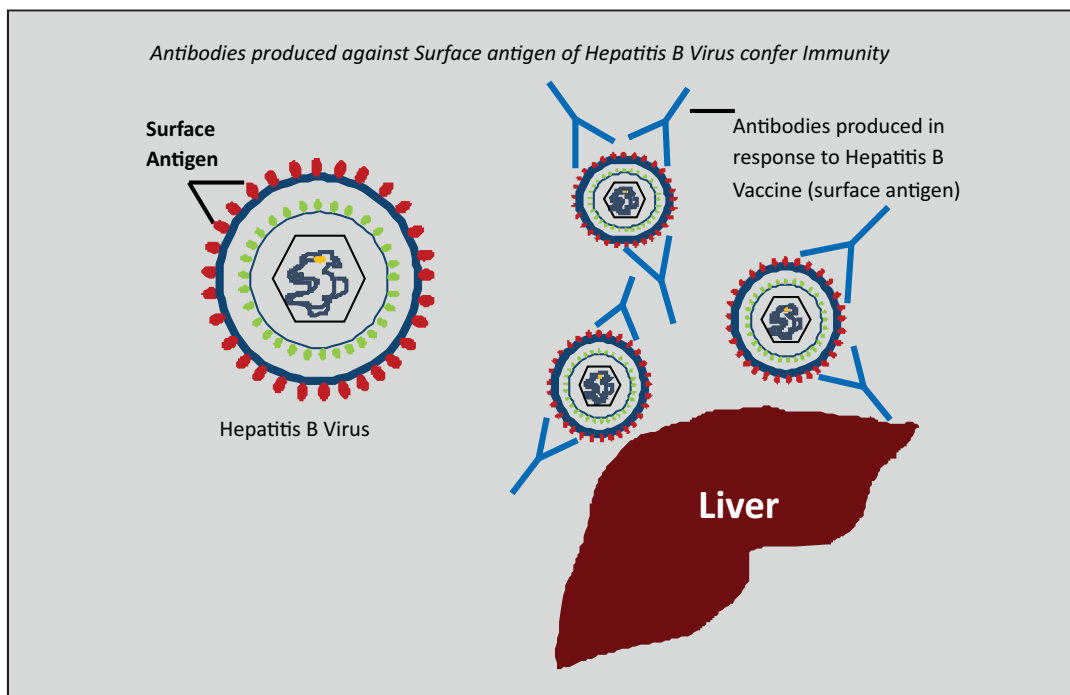
*(Photo Courtesy: K. Varaprasad Reddy)*



The next step for the duo was to build the team. Dr. Gita started recruitment of a few bio technicians and put up an initial list of lab instruments and chemicals needed for their venture. Varaprasad, now in a leadership role, wrote a patriotic letter to the Indian scientific community requesting them to come and join the cause of making India free from hepatitis B. "I wrote to about seventy researchers, and out of those, only three responded. They came back to India and joined Shantha. Soon, we had a team of 4-5 people led by Dr. Gita", recollects Varaprasad.

Shantha's team at Osmania started working on hepatitis B vaccine and interferon projects simultaneously. Meanwhile, Varada introduced him to Dr. Guntaka Rami Reddy, an alumnus of Banaras Hindu University and a microbiologist who was running his own research laboratory at the University of Columbia, Missouri, USA. Varaprasad visited the USA and met Dr. Guntaka, who offered to host and mentor Dr. Gita in his lab. With his support, Dr. Gita could isolate the hepatitis B surface antigen by the end of 1993.

Surface antigen is a small molecule present on the outer covering of a virus's body. Surface antigen, when injected alone in the human bloodstream, provokes the immune system, and antibodies are produced in the body. Specific antibodies are produced against specific surface antigens. Once produced, these antibodies stay in the human body forever, and provide protection against the virus in the event of an infection. This is how vaccinations work.



*Hepatitis B surface antigen induced immune response (Graphic by Adita Joshi)*

For producing a recombinant vaccine, the surface antigen DNA needs to be inserted into the DNA of a host organism. Amongst the host organisms used for vaccine production, bacteria and yeast are popular. Once the recombinant clone of the host organism is ready, it is grown in large-scale in a liquid medium that acts as food, and the cells are processed to purify the surface antigen which is produced inside the cell. The purified antigen is formulated for use as a vaccine. Isolation of hepatitis B surface antigen DNA in 1993 was a huge leap for Shantha; it was the first successful step towards the development of the vaccine.

### The problem of 'Precedence' and comrades from the Middle East

While the scientists were doing their job on the research front, finances, or the lack of it, was a major worry for Shantha Biotechnics. The initial seed money of 1.9 crores was running out, and more money was needed for taking the next big step – expression studies of the surface antigen. Varaprasad contacted many banks and none of them had heard about recombinant DNA as a business venture. In his argument supporting the need to invest in hepatitis B vaccine, Varaprasad wrote – “WHO statistics say that more people die because of hepatitis B in



a day than due to AIDS in a year. There is no solution for AIDS, but we have a solution for Hepatitis B.” But banks could not entertain his loan request as there was no precedence of funding for a recombinant DNA product being developed in India.

The fact that there was no prior venture on recombinant DNA technology turned out to be a major stumbling block for Shantha Biotechnics – from getting the license approved to requesting for a bank loan or getting the bureaucratic process to run smoothly. Shantha's initial experiences today make Varaprasad oppose precedence. “Precedence should be removed from dictionary. Innovation happens only when there is no precedence”, he says. Innovation was indeed the axis around which Shantha's mandate revolved. Innovation enabled the company to spin off eleven recombinant products in future that successfully paved their way into the market.

A silver lining in the dark cloud of financial trouble appeared for Shantha from Oman in the Middle East. It is intriguing to know what spurred Oman's involvement and interest. Varaprasad, who had strong literary inclinations, was also close to Mr. P.V Narsimha Rao, former Prime Minister of India, also known for his penchant for good literature. When Mr. Rao was a foreign minister in Oman, he had made friends with the Omani Foreign Minister Yousuf Bin Allawi Abdulla. Few years later, in a candid conversation with Abdulla, Rao mentioned to him about Shantha Biotechnics and hepatitis B. The Omani minister became instantly engaged, and was impressed with the possibility of the healthcare impact that Shantha was

attempting to achieve through the development of hepatitis B vaccine. In 1994, Yousuf Bin Allawi Abdulla and his representative Khalil Ahmed, visited Shantha Biotechnics and bought 50% stake in the company with an investment of Rs. 1.9 crores. In addition, Abdulla arranged for additional capital through loans at low rates from banks in Oman.

With the Omani investment coming in, things started rolling quickly for setting up a state-of-the-art factory for mass scale vaccine production. Though Shantha Biotechnics now



*K. Varaprasad Reddy, Dr. Gita Sharma and Omani Foreign Minister Yousuf Bin Allawi Abdulla in the year 1994*

*(Photo Courtesy: K. Varaprasad Reddy)*

had the money, none of the researchers had any idea about how a mass scale production plant should be designed! Help came in the form of Dr. P.M Bhargava, the Founder Director of Centre for Cell and Molecular Biology (CCMB) and his associate, Chandana Chakrabarty. They were then providing consultancy to pharma companies. They arranged for Shantha Biotechnics, a visit to the newly laid R&D centre and production plant of Sun Pharmaceuticals at Baroda. The visit helped Shantha's staff understand the infrastructural details of a production facility.

“While there are indifferent people, there are sensitive humans as well”, Varaprasad recalls. He fondly remembers the encouragement and support given by Dr. Harshvardhan, the then Health Minister, who supported the company's license application. Yet another support from the government came from Technology Development Board (TDB), established by the Department of Science and Technology (DST). In fact, the first application that made its way to TDB was from Shantha Biotechnics. In the year 1996, TDB supported the company with a grant of Rs. 8 crore, which was utilized to set up large-scale production facilities.

### **Moving places, finding a home and getting settled**

Shantha's initial years were a bumpy ride. Before Varaprasad could relax and utilize the newly acquired financial help from Oman, he discovered the institutional discomfort brewing at Osmania. Those were the days of intermittent power supply, and the R&D lab was equipped with an air conditioner that would run on a generator in the event of a power failure.



*The first batch of scientists from CCMB visiting the factory site of Shantha Biotechnics in the year 1995*

*(Photo Courtesy: K. Varaprasad Reddy)*

Dr. Malla Reddy could sense the difficulties and was wise enough to foresee that the situation might slow down the company's work. He advised Shantha Biotechnics to vacate the lab at Osmania. The factory being still under construction, the company was desperate for a new home. Dr. Guntaka suggested exploring CCMB to find space. Dr. Bhargava introduced Varaprasad to the then Director of CCMB, Dr. Balasubramanian. "Balasubramanian was a strict administrator; he welcomed Shantha Biotechnics to CCMB but with a staff cap of not more than 8 people, and a rent of Rs. 1.25 lakhs per month", recalls Varaprasad. Balasubramanian's strict attitude turned out to be a blessing in disguise as it positively propelled the company to speed up the process of getting the factory ready and be independent.

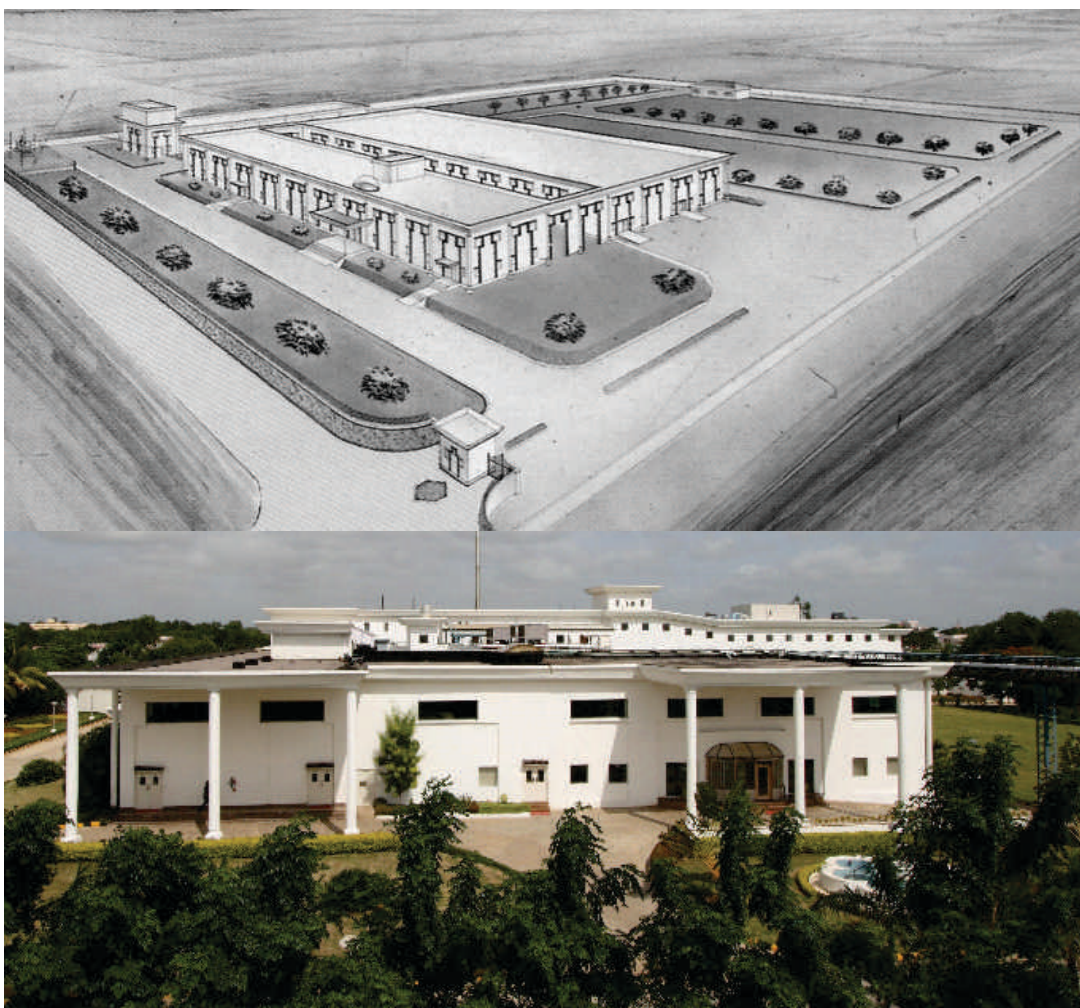
Shantha Biotechnics' year and a half stint at CCMB was a memorable one with an ambience full of tranquility, intellect, association, and collaboration. Dr. Gita chose not to leave her job at Osmania and handed over the initial work to Dr. K.S.N. Prasad of CCMB, a former student of Bhargava. With this, the last connect with Osmania was lost and the company embarked on a new association with CCMB. Dr. Revathi, a scientific officer at CCMB also came on board. Talking about work done at CCMB, Dr. Revathi comments, "Shantha Biotechnics conducted the critical characterization (series of quality tests needed after an antigen is cloned) of the hepatitis B surface antigen (HBsAg) at CCMB." She also mentions that many state-of-the-art facilities such as electron microscopy, CD spectroscopy, and DNA sequencing were made available to the company's R&D unit at CCMB. She fondly remembers Mr. Jayaraman, a staff working at the Animal House facility of CCMB for his kind help. CCMB provided the company with intellectual handholding, scientific endorsement, infrastructural support and alignment in the right direction. In October 1995, it moved out of CCMB to its own R&D facility.

## **Shanvac B – India's first indigenous vaccine against hepatitis B**

In the spring of 1996, the company's first batch of recombinant DNA hepatitis B vaccine – Shanvac-B – was ready after being tested on animals. The vaccine was produced using *Pichia pastoris*, a substance different from the one that some of the successful multinational companies used. Shanvac-B posed a great example of process innovation as *Pichia pastoris* was used for the first time to produce a commercial product. Shanvac-B was decorated with two process patents owing to its better yield and a robust purification method. The next step was clinical trials on humans.

The innovative nature of Shanvac-B got the company embroiled in a tussle with safety committees and regulatory bodies. Since it was the first recombinant DNA product from India, scepticism was rife with regulatory bodies who acted as gatekeepers. The company had to present its case to numerous important regulatory bodies since the vaccine was to be tested

and used on humans. Even today, Varaprasad's face shows signs of exhaustion when he recalls the experiences of getting an approval for human clinical trials. "I found God in one person – Dr. Mashelkar, the then Director General of Council of Scientific and Industrial Research (CSIR)", he says, referring to the contributions of Mashelkar. Finally, Drug Controller General of India (DCGI) approved Shanvac-B for clinical trials and the vaccine was launched on 18<sup>th</sup> August, 1997 as a product synonymous with and symbolizing the progress that India had made in the 50 years of independence.



*The blueprint (top) of the factory of Shantha Biotechnics and the factory (bottom)*  
(Photo Courtesy: K. Varaprasad Reddy)



## Winning over the market competition

After about 4 years of hard work, Shantha Biotechnics finally had the product that it was striving towards. The next challenge to tackle was marketing it at an affordable price of \$1. Traditionally, marketing involves a hidden series of middlemen - retailers, stockists, super-stockists and so on—almost like a set of Russian dolls. The company, new to all this, had no idea of how to market Shanvac-B. The only directive it had was that the vaccine's price would not exceed Rs. 50 per dose. Sensing the impending competition, Smithkline Beecham reduced its price from Rs. 750 per dose to Rs. 520 per dose. Realising an opportunity, the marketing department of Dr. Reddy's Laboratories offered to market Shanvac-B. They suggested that the vaccine should be strategically priced at Rs. 519 per dose with taxes, just a rupee less than the foreign counterpart. With this, the company predicted a revenue of Rs. 50 lakhs for the first six months.

The renewed marketing strategy was definitely not in line with Shantha Biotechnics' original commitment of Rs. 50 per dose. They did not want their dream of an affordable vaccine to go to dust. "We took a blind call and decided to market Shanvac-B ourselves", says Varaprasad. In September 1997, about 17-18 people were recruited for marketing the vaccine. A few doctors came forward to train these recruits, and the training process went on till November. Marketing started in December, and by March 1998, about 1.8 million doses were sold at a price of Rs. 50/dose. This translated to revenues worth Rs. 7.5 crores in the first six months.

Though Shanvac-B was marketed at Rs. 50, the retail price reached Rs. 180 due to commissions of several players involved. Middlemen came out to be the real problem. The company had to find a way to circumvent this hindrance towards realizing the price of Rs. 50 /dose. The company knocked a new door – the Indian Medical Association (IMA) and here, it presented a lecture on the development of Shanvac-B, its efficacy and affordability. Soon the company walked out of IMA with a promise of a mammoth exercise - mass immunization camps.

With the support of All India Medical Council (AIMC), the All India Paediatric Association, district administration and local medical doctors, camps were organized on Saturdays, Sundays and national holidays. Each Sunday, about 30,000 children were vaccinated throughout the country in these camps. The price of Shanvac-B was fixed as Rs. 50 for adults and Rs. 25 for children. About 35,000 doctors participated as volunteers in delivering the 'swadesi' (made in India) vaccine to the children of India. Now, an instinctive decision had given birth to a mass immunisation revolution.

The company's business was growing too. It sold 22 million doses in 1998 followed by 28 and 70 million doses for the next consecutive years. Shanvac-B sales indeed broke the roof.

## SHANVAC-B Launch

The Nizam Institute of Medical Sciences (NIMS), Hyderabad, came forward as a partner for human clinical trials. For human trials, a total of 8 people including Varaprasad, his wife, two daughters and his personal secretary got injected with Shanvac-B. This voluntary act displayed the confidence in the missionary zeal of the company's R&D team and the trust that Indian science could produce a recombinant DNA product.



*(Photo Courtesy: K. Varaprasad Reddy)*

Phase I trials for checking the product's safety were completed successfully. Phase II trials for testing the efficacy of the vaccine were conducted at NIMS and King Edward Memorial Hospital in Mumbai. The results of these trials were released in April 1997 and Shanvac-B was announced to be the poor's solution for Hepatitis B. The year 1997 had also marked the 50<sup>th</sup> anniversary of an Independent India. The then Prime Minister, Mr. I.K. Gujral, had agreed to allow the launch of Shanvac B on the occasion of India's 50<sup>th</sup> Independence Day. However, the thought could not be materialized due to other political, social and business commitments of the leaders.

Finally, Shanvac B was launched as India's first genetically engineered human healthcare product on 18<sup>th</sup> August, 1997 by Mrs. Renuka Chaudhary, the then Union Minister of State for Health, and Prof. Y.K. Alagh, the then Union Minister of State for Science and Technology, in the presence of Dr. N. Janardhan Reddy, Minister of Medicine and Health, Andhra Pradesh.

## The necessary evil – Regulations and permissions

With a grand success in India, Shanvac B was all set to make inroads in the international market too. But regulatory bodies and government agencies came in the way. The company's bid to seek duty free status for expensive equipment, struggle with anti dumping act, strife to get an approval for human and animal clinical trials – all of them were a daunting task.



During the scuffle, the company lost an export order from Russia since it was still waiting for an export permit from the Directorate General of Foreign Trade (DGFT), to ship the vaccine consignment. In addition, for any vaccine to be exported, it needed to be evaluated for quality at the Central Research Institute in Kasauli, Himachal Pradesh, which took about six months to get this whole process done. Although the export consignment was ready, this delay made the Russians impatient and the company lost the order.

### WHO Prequalification

It is a process that aims to ensure that diagnostics, medicines, vaccines and immunization-related equipment and devices for high burden diseases meet global standards of quality, safety and efficacy, in order to optimize use of health resources and improve health outcomes.

The prequalification process consists of a transparent, scientifically sound assessment, which includes dossier review, consistency testing or performance evaluation and site visits to manufacturers. This information, in conjunction with other procurement criteria, is used by UN and other procurement agencies to make purchasing decisions regarding diagnostics, medicines and/or vaccines.

Source: <http://www.who.int/topics/prequalification/en/>

The delay was experienced when Shanvac-B took a long time to get included in the National Immunization Program. Inclusion in this program meant that children in every village, every town, and every city could be protected. Though countries like Myanmar, Nepal, Pakistan, Bangladesh and Sri Lanka had already included hepatitis B in their immunization program, India took a long time of 14 years to include this disease in the immunization program. By 2011, when this was included, Shantha Biotechnics had already proved its mettle by winning the National Technology Award, many state and national level awards, the WHO prequalification, and even a Padma Bhushan for its founder.

### Allegations and a face-off

The company's hepatitis B vaccine received good publicity, but the existing multinational leader in vaccines continued to get most of the market share. Though many doctors in private practice were using Shanvac-B, they priced it on par with the vaccine from a multinational.

Some continued to be loyal to the multinational company and would often mention issues with the safety and efficacy of Shanvac-B. The vilification campaign against Shanvac-B boiled and finally condensed when the DCGI, Mr. Dasgupta, called upon Shantha Biotechnics' senior management and announced reconsidering the safety and efficacy of Shanvac-B. An unmentioned threat of getting Shanvac-B's license revoked loomed over the company. The management retorted instantly by questioning what prompted DCGI to give a license in the first place if it did not believe in the quality of Shanvac-B. The argument was difficult to win over; and along with the company's, the DCGI's credibility was also at stake. The only plausible solution was to compare Shanvac-B with its international counterpart.

In a series of comparison studies that followed, it was found that both the vaccines were similar with respect to the protection they could offer. However, a study published in the journal *Vaccine* in 1999 found that Shanvac-B was far more superior to the others in its efficacy. This success stood tall on the pillar of technology that was employed in the production and purification of Shanvac-B, and the scientific minds that created the success recipe.

Realizing the potential in the biotechnology sector, many companies followed suit and Shantha Biotechnics started facing competition from new entrants in and around Hyderabad. It had given these new companies the most sought after gift - precedence. The regulatory roadmap for national and international business involving recombinant DNA had evolved with the company's advancement. Following Shanvac-B's success, the licensing authorities were less critical of recombinant DNA products. A few companies started questioning and criticizing the company's process innovation using *Pichia pastoris* and complained about low yields of recombinant product using the process. They totally ignored the cutting edge downstream purification technology which the company had standardized. The competitors could use *Pichia*, but since the final product is only 3-5% of the total mass, one needs a very efficient purification system for obtaining best yields. Dr. P.M. Bhargava intervened and highlighted the importance of downstream processing and purification to be a major area where a vaccine manufacturing company's R&D should focus. He endorsed the purification and quality control standards developed by the company.

Another vaccine manufacturing company questioned and argued about the relevance of WHO prequalification certificate for marketing a vaccine under the pretext that India has its own licensing authority in the DCGI. This matter ended up in the court of law. The CEO of the contesting company was asked if they had ever tried to apply for the WHO prequalification. It was revealed that the company had tried for four years and had failed to receive it. The presiding judge closed the matter by saying that he was unable to give judgment on which license is better. All he knew for sure was that if WHO was not good, the opposing company

would have not applied for a prequalification license, that too four times. In Varaprasad's words, "The Judge dealt the matter with utmost wit – the snake did not die, and the stick did not break."

## Progress by leaps and bounds

As they say, life always comes a full circle. The story of Shantha Biotechnics was not different. The banks that had earlier refused to give loans to the company were now in line to invest in it. State Bank of India's mutual fund, and Morgan Stanley invested 10 million USD in equity, which was to be used towards building up manufacturing facilities. The company also received recognition from the Pfizer, a multinational pharmaceutical company, which came forward as a marketing partner and co marketed Shanvac-B under the brand name of Hepasheid in 2002. By this time, the company catered to about 50% of the world's requirement for Hepatitis-B vaccine for immunization drives. It also exported vaccines to more than 10 countries, with UNICEF as one of its client.

In an article on "*Vaccines: weapons of peace and prosperity*" published by The Hindu on July 1, 2004, the company found a profound mention. A segment from the article read – "*Hepatitis B vaccine, in a sense, can be thought of as the harbinger of recombinant DNA biotech in India. Shantha Biotechnics, based in Hyderabad, produced HBV in 1997 and successfully competed with multinationals and brought the price down more than hundred-fold. Today Shantha not only offers affordable HBV to India but regularly sends it to African nations and, remarkably, to Pakistan. Vaccines are indeed weapons of peace, as Dr. Peter Hoetz remarked in his review in EMBO Reports of October 2001.*"

In Pakistan, hepatitis B and C have emerged as dreadful healthcare problems with every 13<sup>th</sup> Pakistani infected with either of the viruses. Varaprasad recalls, "In 1999, when India started the Delhi-Lahore bus service to Pakistan, I informed Shri. A.B. Vajpayee that Shanvac-B is exported to Pakistan for their children as a token of friendship."

## Commitment to innovation

One thing that stood out in the way Shantha Biotechnics functioned was its passion for innovation. At that time, the only competitor that manufactured a similar vaccine against hepatitis B was Merc R&D, which used *Saccharomyces cerevisiae* (yeast) for expression. "Shantha worked on expression and purification of eleven recombinant proteins, we exhausted everything respecting the patent environment", recalls Dr. Revathi Chaganti, a Scientific Technical Officer at CCMB, who later joined the company.

Shantha Biotechnics also established a cell bank of HPV vaccine for a US based company under a contract research project. The backbone of the company's product quality was the robust purification pipeline which was developed by the team consisting of Dr. Revathi, Dr. Sriram, Dr. Venkataramana, Vijayrangam and Sudhir. The process made sure that the final drug substance was free of impurities and other interfering agents.

When asked about other projects, Dr. Revathi fondly remembers, "Oh, there were many projects; at one time we had nearly sixty projects. All ideas that could connect with cost effective improvement in Indian healthcare were incubated. The management gave importance to all such ideas akin to how a gardener prunes, nurtures and allows every bud in his garden to bloom." The company made a policy to invest 12-25% of its profits back into R&D to support innovation of new products and kept launching one product every two or three years. It undertook projects on rotavirus, pneumococcal, varicella, meningococcal, DPT and Hib vaccines. Many of these projects were international collaborations. Owing to its innovation and product quality, the company has obtained WHO prequalification for four vaccines – Shan5-a pentavalent pediatric vaccine, Shanchol – a cholera vaccine, Shanvac-B-hepatitis B vaccine, and Shan TT- tetanus vaccine.

The company's product quality attracted international players for clinical collaborations. The International Vaccine Institute in South Korea requested the company's participation in conducting clinical trials for its oral cholera vaccine. The internationally licensed cholera vaccine was priced at \$18 per shot in India. Within the ambit of this collaboration, the company was successful in bringing down this price to \$2 per shot. It also ran a clinical trial (phase I) for paediatric dengue vaccine.



*Shantha Biotechnics was awarded with the National Technology Award for the year 2003*

*(Photo Courtesy:  
K.I. Varaprasad Reddy)*

“Shantha's process innovation continued seamlessly for another product called Interferon alpha 2b”, recalls Dr. Revathi. Interferon alpha 2b is administered clinically to cancer patients.

### Dr. Revathi Chaganti

Shantha Biotechnics' face of scientific talent

Dr. Revathi, a Scientific Technical officer at CCMB, who later joined Shantha Biotechnics played a very pivotal role in shaping the company's future. She joined Shantha in 1999 after working with the company for about one and a half years on deputation for a CSIR-Industry collaboration project. “It was quite a difficult decision”, says Dr. Revathi, to leave a government job at India's most premier research institute for a nascent private company was being laughed at initially by her colleagues. But she never had to look back.



Dr. Revathi was one of the few people who had known the company's mandate ever since it was incubated at CCMB. She says, “Applied work, clinical trials, vaccines, affordable healthcare, recombinant products for masses—all this fascinated me.” She was confident that the holistic training she had received from CCMB would be instrumental in realizing her career dreams at the company. Having seen Varaprasad's commitment and resolve, Dr. Revathi took the decision to move to Shantha Biotechnics as she believed that “Founders of any organization are very important.” When asked about her role, she chuckles with an effervescent excitement and says, “I played with recombinant proteins”. Dr. Revathi was involved with expression and purification of the interferon alpha 2b, which after facing a few challenges, was launched as Shanferon in 2002. Shanferon too joined the affordable bandwagon of healthcare products, being priced at Rs. 300 as compared to the international version available at Rs. 1200. It was another example where Shantha's R&D had experimented in expressing interferon for the first time in a host expression system other than bacteria. Both Shanvac B and Shanferon won the National Technology Award for the years 1999 and 2003, respectively.



## New beginnings, erstwhile philosophies

The company's role within international collaborations and its potential for growth in the biotechnology sector in South East Asia attracted Merieux-Alliance, a vaccine manufacturer from France. In 2006-07, when Shantha Biotechnics was poised to have a turnover of about Rs. 100 crores, Merieux bought 50% of shares of the company that was previously owned by the Omani partner, and another 10% held by another stakeholder. This acquisition was aimed at grounding Merieux's Asian presence, and turning Shantha Biotechnics into its worldwide vaccine production centre. Post this acquisition, Varaprasad continued as the Managing Director, and Khalil Ahmed as the Executive Director. Georges Hibon, Director of Merieux, was now the Chairman of Shantha Biotechnics.

Rather than investing into entrepreneurship ventures and therapeutic proteins, Merieux established a mandate of focusing on vaccine production. It retained Shantha Biotechnics' name and its philosophy of affordable healthcare products. In its first move, Merieux focus was to upscale the hepatitis B vaccine production. This opened up new markets for the company, and about 60% of its revenue could be attributed to exports. A USD 340 million contract from UNICEF for pentavalent vaccine, Shan 5, added to its glory.



*Shantha Biotechnics- Merieux-Alliance (France) merger in 2006*

*(Photo Courtesy: K. Varaprasad Reddy)*



With innovation at its forefront, the company was attracting a lot of international attention. A lucrative offer from the world's largest vaccine manufacturer, Sanofi, was a big breakthrough in the company's journey. Sanofi Pasteur, the vaccine producing arm of Sanofi, was already a leader in the European market and was looking at expanding its presence. Merieux, who had been a previous partner of Sanofi, suggested Shantha Biotechnics as a possible 'Southern innovator'—a name popularly given to biotech companies in South East Asia.

In 2009, Sanofi Pasteur acquired the 80% stake owned by ShanH, a subsidiary of Merieux Alliance, in Shantha Biotechnics, valued at about Rs. 3,783 crores. In 2009, the company's sales were expected to be around USD 90 million (Rs. 433 crore). Sanofi-Aventis later acquired Shantha Biotechnics for USD 784 million, a whopping eight times of its value in 2009!

For a company focusing on healthcare innovations for the poor, the equilibrium between keeping products affordable and the company profitable needs to be skillfully maintained. "I did not learn as much about management after I obtained my MBA degree, as compared to what I had learnt in setting, nurturing and growing Shantha. Life experiences and unexpected situations are the best management gurus; they teach us skills that are probably not written down in any coursework", says Varaprasad.



*Shantha Biotechnics- Sanofi merger in 2009*

*(Photo Courtesy: K. Varaprasad Reddy)*

The company's accomplishment can be attributed to its decision in seeking partnerships from international sources. Domestic financing for R&D was not easy to obtain due to high risk and low returns in those days. As Varaprasad recalls, "Post the success of Shanvac 5, the

### **Shantha-Sanofi: New strides in affordable healthcare products**

Shantha-Sanofi has set a record by delivering 10 million doses of its cholera vaccine, Shanchol, in October 2017. Shanchol received WHO prequalification in 2011 and is exported to 25 countries. The current shipment will be utilized for vaccination in endemic areas and is expected to protect 5 million lives from cholera.

Shantha-Sanofi has supplied 20 million doses of the injectable polio vaccine, Shan IPV, from 2015 till October 2017. Shan IPV is the only inactivated polio vaccine (IPV) to be manufactured in India using the technology obtained from Sanofi-Pasteur. The Indian government has introduced one dose of IPV at 14 months of age in addition to the oral polio vaccine in the National Childhood Immunization Program.

A new vaccine production facility was constructed in Muppireddipalli, Hyderabad, with an investment of Rs. 250 crore in 2016. The facility got regulatory approvals from the government as well as WHO. The facility was set up for mass production of Shan5 and Shanchol. Another plant in Medchal has a capacity of producing 400 million doses of vaccines.

In 2015, Telangana's Chief Minister, K Chandrasekhar Rao, laid the foundation stone of a Rs. 460 crore insulin manufacturing facility for manufacturing Insuman, a leading human insulin product for diabetes treatment. This will be Sanofi's second Insuman manufacturing plant, the first being located in Frankfurt. The building is under construction and is projected to be around 13,400 square-metres and will be operational by 2019.

Shantha-Sanofi received WHO prequalification in May 2014 for its pentavalent vaccine Shan5, which provides protection against diphtheria, tetanus, pertussis, Hib and Hepatitis B. The company aims at a revenue of about Rs. 500 crores from the re-launch of Shan5. About 18 million doses of Shan5 were sold in the years 2008-10. In 2010, WHO had withdrawn the prequalification for the earlier version of Shan5 due to sedimentation issues in the vaccine vials.

The company has also produced the first indigenously developed four-in-one vaccine, Shantetra which offers protection against four infectious diseases - diphtheria, tetanus, pertussis and hepatitis B. Shantetra was sold at a much lesser price compared to the multinational three-dose DTPH being marketed at Rs. 225 per dose.

management started considering a public issue for the company, but I was not convinced. R&D business does not offer early outputs akin to IT business. There was a major risk of people losing their money having invested in public issue of an R&D venture. For Shantha, unconventional financing worked.”

Shantha Biotechnics' evolution as a recombinant- DNA product based company is incredible. It was the foundation stone for the evolution of Hyderabad as a biotechnology hub. Today's Hyderabad is a one-stop shop for the biopharma sector. A number of biotech parks, companies and contract research organizations started sprouting in Hyderabad after the company set a precedence.

Now a Sanofi company with world-class production facilities, Shantha Biotechnics can give any competitor a chill down their spine. Varaprasad continues to be the Chairman of the company. He professes that the takeover was benevolent as Sanofi understands and endorses the philosophy on which his company was set up. The story of Shantha Biotechnics is indeed a remarkable example of unmatched accomplishment of those that were once being scoffed at for scientific incompetence. Today, they are indeed the torchbearers for vaccine production.

Shantha Biotechnics' story is not an easy one to live or emulate; it takes a lot of courage and motivation to venture in an unknown territory and dig gold from an unfamiliar ground. This is one of the many stories that highlight the dedication, passion and excellence of Indian scientists.

## Acknowledgements

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**1992**

Varaprasad (Founder of Shantha Biotechnics) learns about Hepatitis B in a WHO (World Health Organisation) conference in Geneva

**1993**

Gene Sequence of Hepatitis B virus DNA antigen isolated at Shantha Biotechnics



**1996**

First batch of Recombinant DNA Hepatitis B vaccine, **Shanvac-B**, is ready after being tested on animals

**1999**

Shantha Biotechnics wins the National Technology Award



**2002**

Pfizer signs up as a marketing partner for Shanvac-B



**2006**

Mereix buys 60% shares in Shantha biotechnics



**1993**

Motivated by the idea of making Hepatitis B vaccine available to people of India, Varaprasad establishes Shantha Biotechnics



**1994**

Life saving funding from Omani investor Yusuf bin Allawi Abdullah (50% investment)



**1997**

Shanvac-B is officially launched after successful clinical trials



**2001**

The Shanvac-B obtains WHO prequalification



**2003**

Shantha Biotechnics wins the National Technology Award once more



**2009**

Sanofi acquires Shantha biotechnics





## Test before taste: Finding Basmati's identity

By Adita Joshi

Smell is not just a biological and psychological experience; it is a social and cultural phenomenon, too. Take for example the Ongee tribe of the Andaman Islands – the most aromacentric community in the world. For them, the Universe and everything in it is defined by smell. The Bororo of Brazil, an indigenous tribe, and the Serer Ndut of Senegal associate personal identity with smell. Recent studies<sup>1,2,3</sup> on olfaction have thrown some light on some of the exciting qualities of this powerful sense. In many cases, smell has been shown to define identities, and a new field of research called olfactory fingerprinting is born.

But, can smell really define someone's or something's identity? Yes, says research<sup>4</sup>. If you are familiar with the Indian kitchen, this may not be very surprising. The aroma of spices makes up most of our food and what's better to go with this food than a bowl of aromatic Basmati rice? Yes, 'Basmati' – soft, silvery white, long, slim grains with a specific aroma. But did you know that this well-known Basmati, in spite of having a distinct aroma, went through an identity crisis of sorts? Here is the story of Indian Basmati, which had to fight the toughest battles to remain 'Indian' and 'Basmati'.

### Basmati – The queen of rice

The name 'Basmati' is derived from the Sanskrit word 'Bas' or 'Vas', which means 'smell' or 'fragrance', and is amalgamated with 'mati' – a connotation that implies femininity, and also signifies a trait which is 'inborn'. There is also a famous folklore that talks about the aroma of Basmati – a shopkeeper from Punjab had purchased this rice and while it was cooking, the

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<sup>1</sup> Schwartz, S. Sense of smell is strictly personal, study suggests. *ScienceNews* June 22, 2015.

<sup>2</sup> Coppin, G., Pool, E., Delplanque, S., Oud, B., Margot, C., Sander, D. and Van Bavel, J.J. (2016). Swiss identity smells like chocolate: Social identity shapes olfactory judgments. *Scientific Reports* 6:34979.

<sup>3</sup> Canniford, R., Riach, K. and Hill, T. (2017). How smell constitutes meaning, identity and temporal experience in spatial assemblages. *Marketing Theory* <https://doi.org/10.1177/1470593117732462>

<sup>4</sup> Identity verification: Body odor as a biometric identifier, *ScienceDaily* February 4, 2014.



strong aroma apparently diffused in the whole village and spread the news of arrival of Basmati.

Apart from its smell, what makes Basmati the most sought after rice variety is that during the process of cooking, unlike other varieties of rice, though the grains double up in size, their slenderness remains unaltered. The grains are non-sticky, do not break, and remain separated from one another due to the high amylopectin and amylose – two components of starch commonly found in rice.

The home to traditional Basmati is the North and North Western belt of the Indian Sub –continent including the foothills of Himalayas in Uttarakhand, Punjab, Haryana and Pakistan. The climatic conditions and Himalayan waters in these geographical areas are crucial for the aroma. Basmati from these areas, when grown in other geographical locations, loses its aroma. Thus, the geography has a part in the making of Basmati. In addition, in order to belong to the patrician 'Basmati clan', the crop grown should have parents, grandparents and great grandparents as traditional Basmati.

But not every aromatic non-sticky rice is Basmati! An example is Pusa 1121, which qualifies as a Basmati based on elongation and aroma. However, it is not considered to be a real Basmati variety based on the family tree information, as none of its parents is a traditional Basmati variety.

So what exactly qualifies as Basmati? The lack of a specific answer for a long time is the source of the 'identity' crisis that Basmati went through – entangled in a patent war, subjected to rampant adulteration and a source of concern for India's export market.



*Cooked Indian Basmati Rice*

(Photo Credit: By Brian Child - Cilantro Lime Rice, CC BY-SA 2.0, <https://commons.wikimedia.org/w/index.php?curid=41139851>)

## Bio piracy and the theft of Basmati identity

The taste, aroma and the texture of Basmati has made India a prominent exporter in the international Basmati market since the 18<sup>th</sup> century, when it was introduced to the Middle East by Indian traders. Today, India accounts for over 70% of the world's basmati rice production<sup>5</sup>. But, there was a time when we almost lost our Basmati to the West.

In the year 1996-97, Rice Tec Inc., a company based in Texas, USA, had applied for a patent on the ownership over aromatic rice that was bred and grown outside of India, as 'Basmati'. A patent is a licence conferring a right, or title, for a set period, to exclude others from making, using, or selling an invention. Hence, if approved, the international market could be flooded with 'Basmati' rice that is not grown in India and has no parentage of Basmati. While Basmati has been traditionally grown in India for centuries, our rice farmers never documented each and every tweak, trick and tradition that had gone into cultivating the Basmati. Hence, they never applied for such a stamp of law!

The U.S. Patent and Trademarks Office (USPTO) approved a patent application by Rice Tec Inc in September 1997. Suddenly names such as 'Texamati', 'Kasmati' started echoing in the international rice market. About twenty claims on Texamati, Kasmati, and Jasmati as novel aromatic varieties that could be grown outside the Himalayan region and their superior nature than traditional Basmati rice of India and Pakistan were endorsed by the patent. There was a repeated downpour of complaints in the offices of Ministry of Commerce, responsible for promoting and developing policies to foster growth of international trade and exports. Reports suggested a possibility of decline in the exports of Basmati rice.

The inscriptions in the Intellectual Property rule book could not bring any sigh of relief for India as the U.S. legislation announced the claims made by Rice Inc as valid. It had also caused a brief diplomatic crisis between India and the United States, with India threatening to take the matter to the World Trade Organization. The resilient Indian leadership turned the fight to nomenclature claims and a term called 'Geographical Indicator' (GI) helped to rescue and retain our ownership of the 'Gem of food grains'. Following a fierce campaign by the Indian Government, the USPTO disapproved 15 out of 20 claims. Consequently, the patent title was amended from 'Basmati Lines and Grains' to Rice Lines Bas 267, RT 1117, and RT 1121.

India has laid down laws in relation to GI under the Geographical Indication of Goods (Registration and Protection Act, 1999). The Intellectual Property Appellate Board (IPAB) approved to register and issue a GI certification for Indian Basmati to Agricultural and

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<sup>5</sup> *Basmati rice industry may revive in next harvest 2016-17: Icra. Business Standard April 3, 2016.*

Processed Food Products Export Development Authority (APEDA) in 2016, after 7 years of the initial application. Under this GI certification, Basmati grown in seven states of India – Punjab, Haryana, Himachal Pradesh, Uttarakhand, Western Parts of Uttar Pradesh and two districts of Jammu and Kashmir – has been included. This would cover the trade interests of farmers in about 77 districts.

### Geographical Indicator (GI)

GI is included under Intellectual property rights (IPR) and offers a protection similar to a copyright or a patent for any given commodity. GI finds its mention in the Trade Related Aspects of Intellectual Property rights (TRIPS) section of WTO.

GI came into effect in 1995 and provides legal protection to products based on their specific geographical origin. A GI tag is helpful in delivering the customer an authentic product as well as allows producers to prosper and protect their trade in the domestic and international markets.

GI tag can be issued for a natural, manmade or handcrafted product that is produced in a specific location utilizing only local resources. A few examples are Mysore silk, Banganapalle Mango of Andhra Pradesh, Nagpur oranges, Odisha pattachitra, Darjeeling tea, Jaipur blue pottery, etc.

### Administrative watchdogs of the Indian Basmati Trade

The Ministry of Commerce is responsible for promoting and developing policies to foster growth of international trade and exports. Director General Foreign Trade (DGFT) and two autonomous bodies - Export Inspection Council (EIC) and Agricultural and Processed Food Products Export Development Authority (APEDA) associated with the commerce ministry, mainly deal with Basmati rice exporters. APEDA provides for registration of Basmati exporters and also fixes standards for export commodities. EIC is the quality control and inspecting authority for products prior to their export, and is empowered to issue certification of quality of export commodities by establishing stringent quality assurance systems.

## **Basmati adulteration – A rampant malpractice**

While the market was resonating with the scuffle between USA and India over the monopoly on the name Basmati, the pre-existing problem of Basmati adulteration with non-Basmati rice continuously raised eyebrows. This was because unscrupulous traders wanted to increase their profit margins by mixing low-cost non-Basmati rice with the most expensive Basmati. Considering that in the European market, Indian traditional Basmati varieties (TB) commanded about \$850 a ton as against about \$500 - \$167 offered to non-Basmati varieties, the profit margins were indeed huge.

In the year 2004, Udyog Bhawan (Ministry of Commerce) and its associated bodies were overflowed with letters of complaints of Basmati adulteration. A number of Basmati exporters approached DGFT and APEDA officials reporting an imminent danger of decrease in export orders of Basmati rice from United Kingdom. The delinquent act of mixing long grain non-Basmati (NB) and Evolved Basmati (EB) – Basmati rice that is genetically modified—with Basmati was rampant, and an open secret. The basmati trade was becoming sick; importers, exporters, international buyers, and scientific regulatory bodies in Europe, each one of them made a representation at DGFT and APEDA about the adulteration menace.

The practice of adulteration peaked up to an extent that the European Union (EU) considered putting several sanctions and regulations on Basmati trade, including reconsidering import duty exemptions. UK agencies were concerned about this and had taken proactive measures. The situation had progressed from acute to chronic such that in 2003 EU considered imposing a £5000 fine on any exporter supplying impure Basmati. A British daily, *Independent*, reported<sup>6</sup> in June 2004 that as per FSA tests, nearly half of all Basmati sold in Britain is contaminated with inferior long-grain rice. Indian Basmati was subjected to regulatory checks by foreign markets and it needed an identification certificate and a mark of authenticity.

So, if India had to provide a certificate of authenticity for Basmati, it should also devise indigenous methods and technologies for identifying the DNA standards for Basmati. The commerce ministry needed tests that could determine distinctiveness of Basmati within its own group and from other rice varieties – a method that was robust enough to tell the difference between Basmati grown in Punjab vs. the one grown in Uttarakhand.

So how does one ascertain that the Basmati on their plate was indeed what it was, and was worth the money paid to buy it? Fingerprinting, a technique from forensic sciences, came to the rescue and DNA fingerprinting of Basmati varieties evolved as an answer.

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<sup>6</sup> Milmo, C. The heat is on: investigators discover that half the basmati rice sold in Britain is adulterated. *The Independent* June 27, 2004.

### European regulations to counter Basmati fraud

The long fluffy Basmati grains are the best complementary partner to the national dish of Britain- 'Chicken tikka masala'. The catering trade in UK was affected in a major way as it was difficult for the customer to believe that varied levels of stickiness in the rice served to them is not because of the cooking method but rather due to adulteration.

The food fraud was indeed lucrative as non Basmati was priced at 70p per kilo versus Basmati that was priced at 1.4 pounds per kilo. Given the magnitude of fraud and the fat profits that the suppliers were enjoying, Britain took the ultimate resolve to do DNA testing of the basmati. 'Test before Taste' was the new mantra to safeguard the market's as well as customers' interests. These developments greatly affected India's foreign revenues as it was one of the prime exporters to the UK, accounting for about 15% of Indian Basmati export.

European Union regulations announced as EC 1549/2004 and EC1234/2007, officially permitted the import of nine Basmati rice varieties Basmati 370, Type-3 (Dehradun), Basmati 217, Ranbir Basmati, Taraori Basmati (HBC-19), Basmati 386, Kernel (Basmati), Super Basmati, Pusa Basmati). These approved varieties even had zero import duty in the UK.

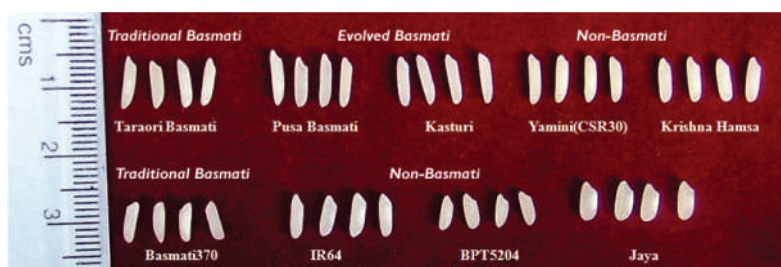
In 2004, the British Retail Council, Indian Rice Association and British Rice Millers Association agreed on the Code of Practice for Basmati which accepted Basmati 198, Basmati 385, Kasturi (IET8580), Haryana Basmati (HKR 228/IET10367), Mahi Suganda, Punjab Basmati (Bauni Basmati) as authentic Basmati varieties. As per the code, the maximum level of non Basmati rice in Basmati was not to exceed more than 7%. The Code of Practice on Basmati rice, in addition, specifies about twenty rice varieties which are not authentic Basmati that can be used as possible adulterants of Basmati.

### Fingerprints of authenticity

In 1998, the Food Standards Agency (FSA) in the UK, in collaboration with the Nottingham University, initiated the first step towards solving the Basmati rice identification problem by developing DNA fingerprinting methods. In 2000, Bligh, a researcher, first reported microsatellite (small repetitive DNA sequences) based DNA-fingerprinting of Basmati rice to test for purity.

Around the same time in India, the watchdogs of Basmati trade in India, took the tales of food fraud in Basmati to the Centre for DNA Fingerprinting (CDFD) in Hyderabad. Here, a group of scientists was working on fingerprinting Basmati varieties.

Before fingerprinting evolved, the physical-chemical tests for authenticating Basmati and differentiating it from non-Basmati varieties involved measurement of about eight to ten different features. One such example is aroma, which is assessed after cooking the rice and smelling it and mostly required a group of experienced experts.



*Grain size comparison of Traditional, Evolved and Non Basmati varieties*  
(Photo Courtesy: Dr. V.V. Sathyawati, CDFD)

However, this kind of testing is subjected to variability or difference of expert opinion over the strength of aroma, as it is a quality trait. The aroma is also dependent on the kind of soil, water, and practices observed while growing the crop and grain maturing. Similarly, verification of other indicators requires a lot of skill, chemical testing and physical examination. These methods offer a certain degree of uncertainty, are a real test of patience, and take up a lot of time.

DNA testing, on the other hand, is certain and undeniable. The environment of the crop or other external factors does not affect the information obtained from DNA. In the case of human fingerprinting in forensics, the patterns of arches, loops and whorls on our fingertips give us a specific identification mark. But, how do we find fingerprints of a DNA?

DNA is a large molecule made up of four units denoted by A (adenine), T (thymine), G (guanine) and C (cytosine). These units are arranged in a linear order in various permutations and combinations to make a DNA sequence. For ease, you may think of an arrangement of beads in four colours (A=red; T=black, G=blue and C=green). A short or long stretch of a DNA may be repeated several times in a row. Now imagine a sequence of four red- two green- three blue- five black beads. If the same sequence is repeated a few or many times, we call it a 'repeat'. The number of these repeats varies from one person to another and thus, is unique for an individual. DNA fingerprinting maps out these unique sequences.



### Centre for DNA Fingerprinting (CDFD), Hyderabad

CDFD was the brainchild of Dr. Lalji Singh, who is known as the 'father of DNA fingerprinting' in India. Dr Lalji's contribution in taking the applications of DNA fingerprinting for solving crimes and paternity disputes was acknowledged by the government and CDFD was born as an outcome in 1995 as a centre dedicated to fingerprinting and diagnostics.

It is an autonomous organization funded by the Department of Biotechnology, Ministry of Science, Technology and Earth Sciences, Government of India. The centre is equipped with world class state-of-the-art instrumentation and computing infrastructure to facilitate working in frontier areas of research in Life Sciences. There are presently nineteen groups working on diverse research areas.

### Basmati finger printing at CDFD

While CDFD rose to fame for its work for testing human DNA samples, there was a group of scientists including M. Kathirvel, R. Ramesh Kumar, and S.E. Hasnain, led by Dr. J Nagaraju, who conducted a study on obtaining DNA fingerprints of Indian Basmati rice varieties. The study was reported in an issue of Proceedings of National Academy of Sciences (PNAS) in 2002. Apart from Indian Basmati, the study also included few varieties from Pakistan.

This work was started in late 1990s, when other countries such as the UK, started their rice variety identification programs using fingerprinting. Though it was not aimed at addressing the concerns of authentication, it did serve as a saviour when the Texamati patent fight urged us to come up with verified molecular signatures, which may highlight the uniqueness and GI quotient of our Basmati varieties, and also when EU came out with a stringent regulation requiring each shipment of rice to have a certificate of authenticity.

As per the DNA fingerprinting protocol developed at CDFD, the scientists identified the varieties Bas 370, Dehraduni, Taraori, Ranbir Basmati and Basmati 386 as authentic Basmati varieties. The study showed that all of these Basmati varieties originated from a single landrace, which is not related to any of the other long grain rice. Other varieties like Basmati 385, Super Basmati, Kernel, Haryana Gaurav, Haryana Basmati, Mahi Sugghanda, Kasturi, Terricot, Sherbati and Pusa Basmati were grouped together as Evolved Basmati (EB). Authentic Basmati, identified this was, was not subjected to plant breeding or genetic modification improvements made for other evolved rice varieties.

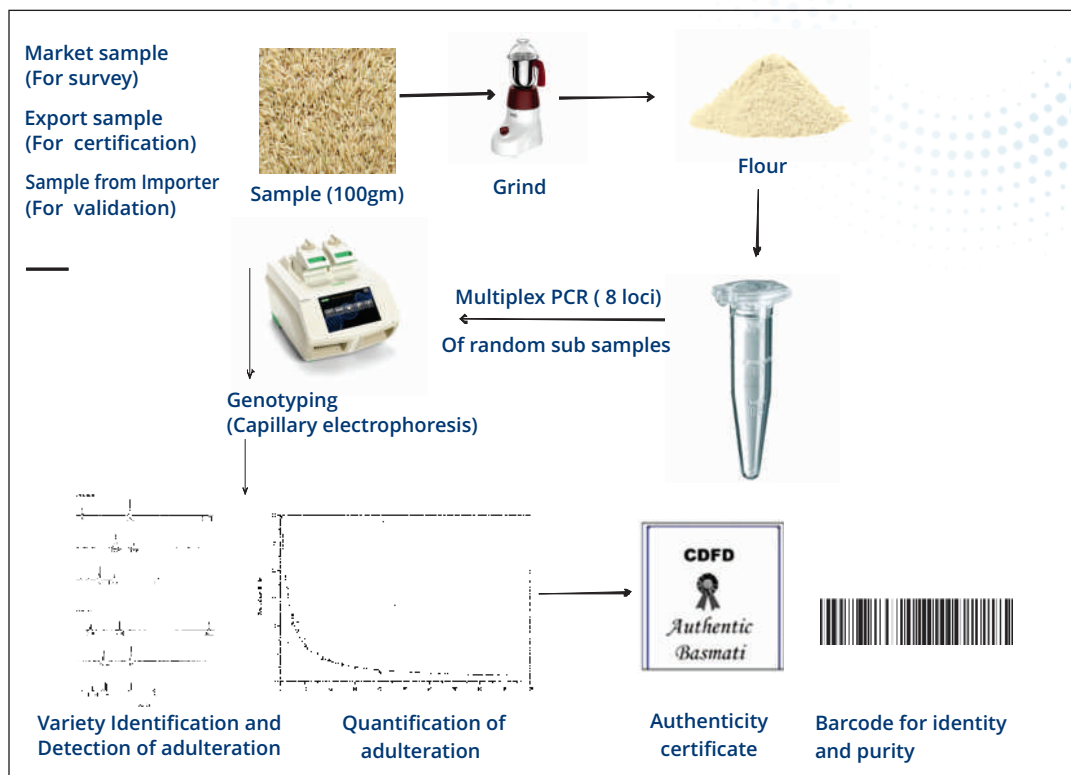
This piece of research work was under advance development stage in 2004 when the Ministry of Commerce and APEDA approached CDFD to develop a testing method, which could distinguish Basmati from other non-Basmati varieties and EB adulterants. This administrative move was an outcome of the EU import regulations. An agreement was signed between Ministry of Commerce, APEDA and CDFD. Subsequently, Basmati Export Development Foundation (BEDF), under APEDA, released a one-time financial grant of Rs 3.5 crores towards setting up a DNA testing facility at CDFD in 2005.



*File Photo of Dr. J. Nagaraju receiving the Technology Award by former President Late Dr. Abul Kalam*

*(Photo Courtesy: Dr. V.V. Sathyawati, CDFD)*

In addition to being foolproof, CDFD's protocol is cost effective too. Just about 100 grams of brown rice sample is required, and the entire cost of analysis is 11,800 INR. The process takes about seven days, and provides a report that specifically mentions the percentage of adulteration of non-Basmati rice in a given sample. The EU regulation allows the percentage of non-Basmati to be less than 7%. The remaining sample is not sent back to the customer, and is with held for about three months just in case there is a need to retest the sample'. APEDA-CDFD management committee devises a set of rules and the certificates are issued in compliance to these specific guidelines.



A layout of the protocol followed by the APEDA CDFD Centre for Basmati Fingerprinting and testing adulteration

(Figure adapted and reconstructed from Lakshminarayana R. Vemireddy et.al . J. Food Sci. Technol. (2015) 52(6):3187-3202)

Minimum Mandatory Characteristics for Varieties of Basmati Rice (Source: British Retail Consortium-Code of Practice on Basmati Rice, 2005)	
	Milled Raw
Minimum elongation ratio on cooking	1.7
Minimum average pre-cooked length	6.5 mm
Amylose content	Intermediate 19-26%
Length/breadth ratio	Greater than 3.5
Gel length	60-100 mm
Alkali spreading value	4-5
Typical Basmati Aroma	Present

<b>Basmati growing districts in India</b> (Source: <a href="http://www.fnbnews.com/Top-News/Basmati-rice-in-India-Its-production-and-export">http://www.fnbnews.com/Top-News/Basmati-rice-in-India-Its-production-and-export</a> )	
<b>State</b>	<b>District</b>
Punjab	Amritsar, Gurdaspur, Kapurthala, Jalandhar, Patiala, Ropar, Nawan Shehar, Fatehgarh Sahib, Hoshiarpur
Uttaranchal	Haridwar, Dehradun, Nainital, Udham Singh Nagar
Uttar Pradesh	Pilibhit, Saharanpur, Rampur, Bijnor, Moradabad, Muzaffarnagar, Badaun
Haryana	Panipat, Karnal, Kaithal, Kurukshetra, Jind, Ambala, Sonapat, Yamunanagar

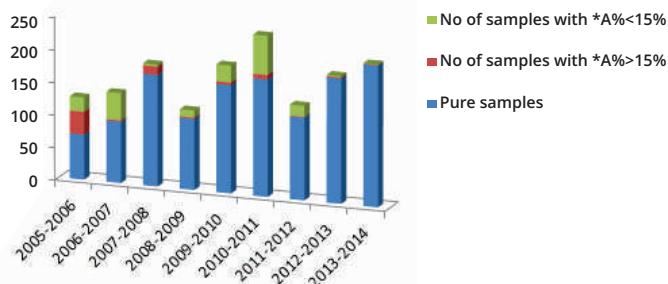
### Impact of fingerprinting on Basmati trade

DNA fingerprinting technology has played a pivotal role in catering to European Union's demand for importing only authentic traditional Basmati from India. About 95,825.06 million tons of Basmati was exported to the UK in 2004-05 and this fell to 84,715.37 tons in the year 2005-06, after the EU regulations came into effect. The streamlining of DNA fingerprinting at CDFD-APEDA centre and issuance of certificate of authenticity for each export shipment of Basmati by EIC helped sustain the Basmati trade with the UK. At the same time other major importing countries also gained a strong confidence for obtaining authentic certified Basmati from India, thus increasing trade, particularly from the Middle East nations.

So how much of an impact did the DNA fingerprinting protocol have on India's Basmati export? "It is very difficult to have an exact calculation as there are other factors such as policies, regulations and international market parameters which may affect the exports, but if I have to make an approximation then there was about 50 % increase in the export after the Ministry of Commerce, EIC and APEDA had laid out the norms and protocols fingerprinting Basmati before exporting", says Mr. A.K. Gupta, Director, BDEF, adding that the technology has definitely curtailed the malpractice of adulteration.

And, how about new challenges? "Once we streamlined the whole protocol for issuing a Certificate of Authenticity, I don't remember any major disputes with any of importing countries", adds Mr. Gupta. He notes that after the advent of the Code of Practice of Basmati fingerprinting, even the exporters (traders, millers, and farmers) gave up the mixing and adulteration practices. "This was a charity they did to themselves to protect their trade interests. The Basmati trade with EU has been doing well since then", he says.

### BASMATI SAMPLES ANALYZED AT APEDA-CDFD CENTRE FROM 2005 TO 2014



*CDFD data showed a considerable decrease in the adulteration percentage over a period of 10 years and a 5% increase in the number of pure samples.*

*(Source: CDFD; Dr. V.V. Sathyawati)*

In addition, APEDA has initiated strong steps towards curbing the malpractice of adulteration in the domestic Basmati rice market as well. “We are working towards putting up a system for mentioning the percentage of non-Basmati for the domestic market to promote transparent labelling. We are registering farmers, traders, millers, and plan to pick up rice samples from mills and markets. These samples will be tested at our laboratory at BDEF, Modipuram. At present, the Evolved Basmati varieties occupy 95% of the domestic market due to better yields and quality. All we want to make sure is that, the customer is paying for what is promised, while protecting the commercial interest of our farmers who are growing the 29 rice varieties notified as Basmati”, explains Mr. Gupta.

Next in the anvil is for the administrators to facilitate the inclusion of more rice varieties including Evolved Basmati (that has at least one of the parents as 'true' Basmati) in the Code of Practice, so that these varieties get a benefit of duty free export. This would greatly improve the trade interests for farmers. The All India Rice Exporters Association (AIREA) is continuously working towards establishing fair practices, curb adulteration, and serve as authentic Basmati suppliers.

### APEDA's EFFORTS TOWARDS IMPROVING BASMATI EXPORTS



*The APEDA -CDFD DNA testing centre was sanctioned on 14 August, 2005 and the MoU was issued on 20 January, 2010. By July 1, 2006 EU made it a mandatory requirement that all the duty free Indian Basmati shipments should be certified for authenticity based on DNA fingerprinting analysis. Export Inspection Council (EIC) in the Ministry of Commerce was the competent body to allot these certificates of authenticity. However, EIC did not have expertise so the tests were outsourced to CDFD.*

The APEDA-CDFD centre, receives the Basmati rice samples from Export Inspection Council (EIC), exporters and importers from India and other countries. The samples are tested for adulteration by using the DNA fingerprinting method developed and standardized at CDFD.

APEDA-CDFD centre is also engaged in identifying regions on DNA that contribute to special characteristics of Basmati such as fragrance, grain elongation, grain width etc. The centre hopes to increase the number of DNA markers to achieve the greatest resolution and accuracy for distinguishing one variety from the other.

APEDA-CDFD centre has standardized single grain analysis for differentiating between several rice varieties. In the year 2015, the centre received and tested about 200 rice samples from EIC. The test developed at CDFD has sensitivity of detection of adulteration from +1% upwards and accuracy of +1.5%. The EU regulation allows the percentage of non basmati to be less than 7 %.

Then, there were six 'traditional' (Basmati370, Basmati 386, Dehraduni, Taraori, Basmati 217 and Ranbir Basmati) and two 'evolved' varieties (Pusa Basmati1 and Super) qualifying as basmati for export from India to UK. All of these were exempted for the import duty of about 78 USD per tonne if they had the certificate of authenticity as per the European Commission regulation 1549/2004.

In November 2008, APEDA had applied to GI Registry in Chennai for registration of Basmati Rice as a GI in order to protect the intellectual property interests of the farmers and exporters. APEDA finally received the GI registration in 2016.

APEDA has established Basmati Export Development Foundation (BEDF) in 2002 at SVBP University of Agriculture and Technology at Modipuram, Merrut. BDEF has a group of agricultural scientists who connect to farmers in the Basmati GI area, conduct awareness for workshops for cultivation of export quality Basmati rice.

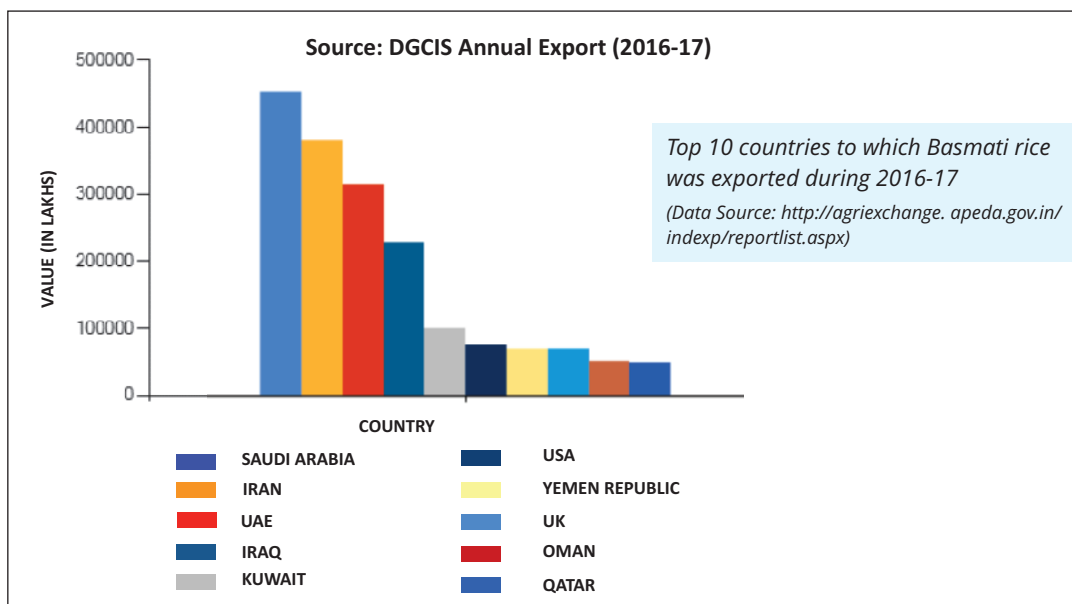
BDEF strategically focuses on strengthening the supply chain by bringing together key stakeholders such as farmers, millers, traders and exporters. BDEF have facilities to test various parameters including testing for pesticides.

## **Basmati trade: Recent trends**

The growth of Basmati trade in the last 10 years has been phenomenal in terms of volume and value (3.5 – 4.0 million tons valued at around 29,000 crore INR). The volume accounts for about 75% of the global Basmati trade. According to the Directorate General of Commercial Intelligence and Statistics (DGCIS), there was an increase from 11.66 lakh tons in 2005-06

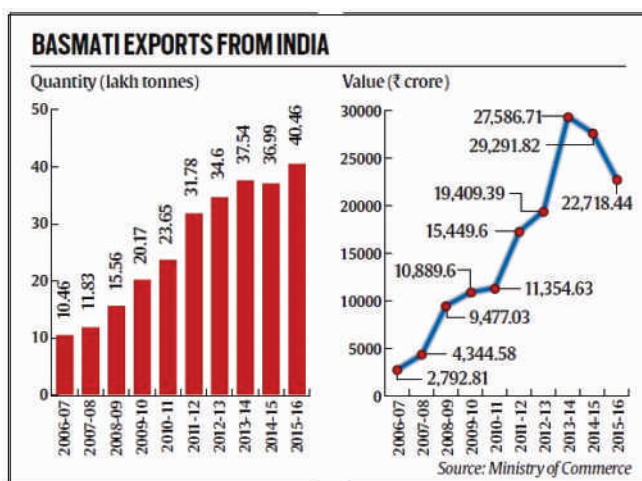


(worth \$687.34m) to 34.59 lakh tons in 2012-13 (worth \$3,564.04m). This was attributed to the dominant role played by the rice exporters in the private sector, breeders who continued to provide progressively improved varieties, and APEDA that facilitated hassle-free trade. Basmati rice exports have increased at a compounded annual growth rate (CAGR) of 27% from 28.24 billion INR in 2004-05 to 275.98 billion INR in 2014-15. The fingerprinting technology greatly facilitated boosting the confidence of importers in procuring high quality authentic Basmati from India.



### Basmati exports from India

(Data Source: <http://indianexpress.com/article/india/india-news-india/basmati-rice-gi-tag-battle-madhya-pradesh-punjab-export-price-agriculture-2994967/>)



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# 7

## SIZZLING FACTS ABOUT BASMATI



1

Basmati, like most other Asian rice, has the biological name *Oryza sativa* and is a true grass belonging to family Poaceae

2

Basmati is the world's most aromatic and fragrant rice. The fragrance comes from a chemical compound named 2-acetyl-1-pyrroline, at a concentration of approximately 90 parts per billion in Basmati



3

Basmati is the highest priced rice in the world



4

Basmati finds its first known mention in the 18<sup>th</sup> century epic 'Heer Ranjha' written by Punjabi poet Waris Shah



5

Basmati rice has a “medium” glycemic index between 56 & 69, making it suitable to consume for diabetics



6

Basmati is usually grown during the months of May to November, when the weather is warm and humid



7

The state of Haryana in India produces more than 60% of the total Basmati rice production in India





## Seeds of fortune: Improved Samba Mahsuri

*By Adita Joshi*

Sitaramaiyah was unwinding himself after a long day's work; his weary eyes gazing at the sky. The clear blue sky of the afternoon had transformed into various hues of grey. The clouds had arrived and Sitaramaiyah was ecstatic. A long wait had been answered. Despite working like a candle burning at both the ends, Sitaramaiyah was barely meeting his crop's demand for water. Now, every single rain drop brought an iota of prosperity for him. After a few showers, his crop looked pristine, full of life. He would stand proudly next to his glistening crop, head held high, with the dignified sense of being a creator. For one moment he would stare at his hands, and the other moment he would gape at his field. The clouds in the sky were waiting to shower more of their blessings, making Sitaramaiyah a very happy man. His self-esteem was evident on his face as a broad smile.

### **A farmer's trouble: Unseen, but known danger**

A few years ago, things were quite different. Sitaramaiyah's fields had not always been a home to the green affluence; they had been attacked by demons of Nature on several occasions—famine, floods, droughts, pests, and cyclones had ravaged his fields before. One such fiendish slap of Nature hit Sitaramaiyah on the afternoon of 12<sup>th</sup> October, 2014. For meteorologists, it was 'Hudhud', named after a colourful bird, but for him, it was a calamity. Hudhud was a cyclone of a very severe nature, which hit Andhra Pradesh's coast at Vishakhapatnam. Post-Hudhud, conditions were ideal for germs and pests, which bloom voraciously after heavy rains, destroying crops. For all coastal farmers like Sitaramaiyah, this catastrophe could have only one possible name - 'death' – dreadful and dark. Of the 7,52,540 households dependent on agriculture and related farming practices were affected; Sitaramaiyah house and farm was one.

Back then, when the cyclone struck, Sitaramaiyah's eyes were still glued to the sky. This time, instead of praying for rains, he was waiting for the heavy rain to stop. The rains had washed away his crops and he had to start afresh on his field. Sitaramaiyah knew that his next struggle



would be to protect his new rice crop from germs and pests. Soon, the clouds dried and so did his courage. He anticipated the upcoming threat of *Xanthomonas oryzae* (Xoo), a bacterium that could cause real trouble. He was sure that *Xanthomonas* would infect his crop; he had experienced huge crop losses owing to the bacterial infection, particularly after heavy rains.

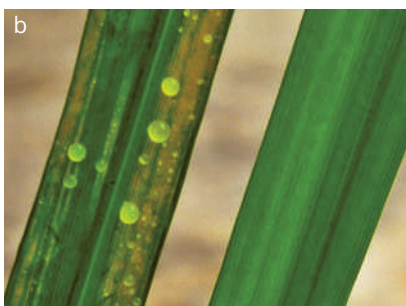
Xoo causes the 'Bacterial Blight' disease in rice, resulting in about 40-50% crop loss on an average. The infection from the bacteria starts at the tip of the leaves, which then moves down the leaf using the plant tissue as a highway, sucking up nutrients as it moves. As a result of the nutrient deficiency, the leaves dry up. A brown spot is often seen on the surface of the leaves; the exit point for the bacteria, after which they enter the irrigation waters and spread on a large scale, or get splashed by rain onto adjacent uninfected leaves. Effective pesticides to kill the bacteria are not yet available for controlling this disease. Thus, once the infection sets in, and weather conditions are favourable, *Xanthomonas* is unstoppable.

Sitaramaiyah's anxiety undoubtedly had a solid ground. The year 2014 had witnessed a major outbreak of the bacterial blight disease in the east Godavari region of Andhra Pradesh. Sitaramaiyah, like many others, had lost his crop to *Xanthomonas*.



*Samba Mahsuri rice variety severely infected with bacterial blight disease post cyclone Hudhud in East Godavari district, Andhra Pradesh*

(Photo Courtesy: Dr. R.M. Sundaram, IIRR)



*Samba Mahsuri rice variety severely infected with bacterial blight disease.  
a) Wilting of the leaves; b) Bacterial ooze which spreads the disease further*

(Photo Courtesy: <http://www.knowledgebank.irri.org/images/stories/bacterial-leaf-blight-1.JPG>;  
<http://www.knowledgebank.irri.org/images/stories/bacterial-ooze.jpg>)



There was, however, a silver lining to Sitaramaiyah's troubles. At the beginning of the crop season, on a small part of his farm, he had planted, on an experimental basis, seeds of a rice variety called Improved Samba Mahsuri (ISM). It was reputed to be resistant to the bacterial blight. Sitaramaiyah found that the part of his farm where he had cultivated ISM was completely free from the disease. He walked over to the house of his friend Venkat, who had also cultivated ISM. Together they surveyed Venkat's fields and found the same scenario. The crop bore its youthful charm with green leaves standing tall. Earlier, Sitaramaiyah and others of his ilk would have dreadful dreams wherein they would see wilting of seeds and yellowing of leaves- an indication of the bacterial blight disease. However, watching their crop stay healthy dissipated their fears. They consulted other friends who had tried out ISM, and heard the same experience, over and over again. ISM was truly resistant to bacterial blight.

Another interesting feature of the new ISM variety, that Sitaramaiyah and Venkat noticed, was an increased tolerance to lodging. Lodging is a phenomenon in which the rice crop bends over near the base of the plant due to winds. This occurs often in coastal areas such as east Godavari that are subjected to high winds and rains towards the end of the crop season. Lodging results in huge crop losses and farmers in east Godavari prefer varieties that are more tolerant to lodging. Increased restraint to lodging indicated that ISM might have a stronger stem than other varieties.

## A bag full of promises

Samba Mahsuri (SM), also known as BPT5204, was originally developed by the Acharya N.G. Ranga Agricultural University (ANGRAU; earlier head quartered in Hyderabad), Guntur, Andhra Pradesh. SM is considered an elite rice variety owing to its high crop yields and extraordinary culinary characteristics. It has a low glycaemic index (GI) of 51.42. Glycaemic index values indicate how slower or faster carbohydrates are digested in our body. Carbohydrates, with glycaemic index lower than 55, are considered good as they bring about lower and slower rise in blood sugar levels. SM is a high yielding variety with a yield of about 50 quintals per hectare. In India, SM accounts for about 3.3% of the total area under rice cultivation. However, its susceptibility to bacterial blight means that developing a resistant variety would have long-term economic benefits, both to the farmers and the country.

At the beginning of the crop season, Sitaramaiyah and a few of his friends had received a 10-kg bag of ISM, each containing enough seeds for cultivation on one acre of land. For Sitaramaiyah and his friends, this was an experiment.

Samba Mahsuri was Sitaramaiyah's favourite crop to grow; a crop that everyone in his family loved. His children loved the taste of it. His wife found it easy to cook. And it fetched good price

in the market, and so obviously he loved it too! Despite this, he was always worried about growing Samba Mahsuri because of its susceptibility to bacterial blight. Now, the results of the experiment were evident. In the despair that followed cyclone Hudhud, there was hope. Sitaramaiyah and Venkat marvelled at this new variety and decided to collect the seeds of ISM from their fields and distribute these 'seeds of fortune' to other farmers.

Sitaramaiyah returned home content, relieved that his crop is protected. His mind filled with the excitement of collecting ISM seeds and popularizing it among other farmers. He had a new business and a new calling in life—to see all the fields in his village and surrounding areas free of bacterial blight. Lying on his cot in the veranda of his house, Sitaramaiyah thought about several questions. Expressions of curiosity and bewilderment would not leave his face. He was curious to know how ISM was developed. What did the seed contain such that *Xanthomonas* couldn't attack the crop? Who are the people who created the ISM variety? With his mind going back and forth on these thoughts and queries, Sitaramaiyah went into deep slumber.

### **From fields to laboratory: The makeover of Samba Mahsuri**

To answer Sitaramaiyah's questions, we need to go back in time, almost twenty-five years back. In 1993, a young scientist, Dr. Ramesh Sonti, joined the Centre for Cell and Molecular Biology (CCMB), Hyderabad. He had earlier worked on genes of bacteria and plants. When asked about his research interests, Dr. Ramesh says, "I was interested in probing the mechanisms by which pathogens or germs (bacteria, viruses, etc.) would interact with plants. I got interested in *Xanthomonas* to understand how it infects the rice plant".

With Andhra Pradesh being one of the major rice growing areas of India, and bacterial blight being one of the deadliest diseases of the rice plant in the region, Dr. Ramesh's choice to study *Xanthomonas* was relevant to the geographical context. "I had neither seen the bacterium before nor grown a rice plant", he says recollecting his motivation for research. During the many meetings with rice breeders and scientists that followed, he met eminent scientists like Dr. Sam Gnanamankan at the Centre for Advanced Studies in Botany, University of Madras, Chennai, Dr. A. P. K Reddy, a rice pathologist at the Indian Institute of Rice Research (IIRR, formerly Directorate of Rice Research [DRR]) Hyderabad, and Dr. E.A. Siddiqui, the Director of IIRR, who developed the first dwarf variety of basmati rice. Dr. Ramesh fondly remembers, "They were very co-operative. They had done basic research on pathogens across rice varieties and had mapped the pathological diversity for infections occurring in the rice plant".

Scientists at CCMB and DRR started the research in 1995 and began to select genes that could confer immunity to rice against *Xanthomonas* species found in India. *Xanthomonas* samples

from various locations were collected and investigated for their genetic diversity using a technique called restriction fragment length polymorphism (RFLP). RFLP is a technique that can map differences (changes) in homologous (similar) DNA sequences. The DNA sequences are chopped into fragments using a restriction enzyme, which acts like a scissor and cuts the DNA at specific places. Based on the variations or changes in a DNA, the restriction enzyme may generate different lengths of fragments for given homologous DNA samples. The differences in the number of fragments based on length describe the variations or changes.

The results of these studies revealed a single lineage of *Xanthomonas*, widely distributed across the Indian landscape. A single strain had penetrated the cultivated rice varieties from Jammu and Kashmir in the north, to Andhra Pradesh in the south, and from Gujarat in the west to Assam in the east. After a few years of additional work, Dr. Ramesh's group, together with the team at IIRR, reported different pathotypes of *Xanthomonas* in India, several of which overlapped with the widely occurring strain. A pathotype refers to all varieties of an organism that infect the same host. In the present case, it would be all types of *Xanthomonas* that infect rice plants to cause the blight disease. Thus, a core collection representing the molecular diversity of *Xanthomonas* was established.

The International Rice Research Institute (IRRI) in Philippines was also involved in a similar research at that time. It had established several strains of isogenic (pure; free of any mutations) rice varieties, some of which contained either one of two genes, *Xa21* and *xa13*, which conferred resistance against most of the *Xanthomonas* strains. Rice varieties with a third gene called *xa5* showed moderate effectiveness against *Xanthomonas*. However, the Dr. Ramesh's group found that the traditional Indian rice varieties that were known to be resistant to bacterial blight pathogen harboured the *xa5* gene. Dr Ramesh says, "Initially we thought that *xa5* was less important, but its presence in all the traditional Indian rice varieties made us consider that it could be a gene of significance".

Success of the unexpected has a thrill of its own kind. Dr Ramesh's speculation about *xa5* proved to be correct. "In the initial surveys conducted by us, *Xa21* and *xa13* genes were found to be resistant to all of the bacterial blight pathogen isolates in our collection. On the other hand, the *xa5* resistance gene did not confer any appreciable level of resistance against these isolates. In spite of this, we went ahead and incorporated the *xa5* gene in Improved Samba Mahsuri because some land races of rice that contained *xa5* are known to have durable resistance against *Xanthomonas*", he recalls. "This was fortunate because subsequently, we have found that *xa5* provides a very good level of resistance against isolates of the pathogen that can break down the resistance conferred by *xa13*. Improved Samba Mahsuri would probably not be resistant against the bacterial blight disease in all parts of the country if we had not included the *xa5* resistance gene", he adds.



*Dr. R.M. Sundaram of IIRR (DRR) and Dr. Ramesh Sonti during the initial evaluation of the newly developed bacterial blight resistant lines. (Photo Courtesy: Dr. Ramesh V. Sonti, CCMB)*

The idea of developing ISM that could confer resistance to *Xanthomonas* was floated in a steering committee meeting of the National Agricultural Technology Program (NATP) under the aegis of the Indian Council of Agriculture Research (ICAR). Based on their background work on *Xanthomonas* diversity and resistance genes in rice, the scientists proposed adding the trio of *Xa21*, *xa13* and *xa5* to the Samba Mahsuri genome to guard it against bacterial blight. Studies from the IRRI, Philippines had already proved that none of the three resistance genes could confer resistance effectively on their own. Either two or all the three genes were needed to achieve resistance.

In the year 1998-99, Dr. Lalji Singh from CCMB and Dr. Paroda, the then Director General, ICAR, presided over the meeting and a collaboration between CCMB and IIRR was proposed. Dr. Prasad Rao, a plant breeder, Dr A.P.K. Reddy, a plant pathologist and Dr. N.P. Sharma, Head of Biotechnology Division, all from IIRR were chosen to be part of the collaboration along with Dr. Ramesh Sonti from CCMB. There were two objectives for this collaboration – one, to create a resistant rice variety using Marker Assisted Selection Breeding (MASB) and Back Crossing, and two, to provide training to IIRR in the technology of MASB using molecular markers.

The idea of improved bacterial blight resistant Samba Mahsuri was thus conceptualized. "Though the Xa21 gene was cloned already, we did not choose to go the transgenic way. There were no ideological decisions or choices. Marker Assisted Selection Breeding was the quickest, non-controversial method to get to the objective. We thought that choosing the non-transgenic approach also would help us getting better public acceptance of the variety", remarks Dr. Ramesh.

### Marker Assisted Selection Breeding:

Marker-assisted selection involves selecting individuals based on their marker pattern (genotype) rather than their observable traits (phenotype). In the case of SM, the scientists were trying to create a new variety that had the 3 important genes rather than qualities like grain size or cooking ability.

Backcrossing is the simplest form of Marker Assisted Selection in which the goal is to incorporate a major gene from a donor plant into an elite recipient cultivar (SM is this case).

### Improving Samba Mahsuri- A beautiful 'vase' of quality traits

While the decision to develop an improved resistant variety of Samba Mahsuri was made, the quest for the 'donor' rice for this exercise continued for a while. A 'donor' is the plant that already has the resistance genes (in this case, the three genes), which are to be introduced into the crop/variety of choice (Samba Mahsuri here). Though there were other rice varieties that were resistant to bacterial blight, none of them had the fine grain and excellent cooking quality characteristics that had hooked farmers to SM in Andhra Pradesh. Despite yield losses due to diseases and pests, farmers chose to continue growing SM with the help of fungicides and insecticides. However, for bacterial blight, there was no such intervention available. For farmers, the best solution was a SM variety that was resistant to bacterial leaf blight disease.

To design the new variety, the donor rice plant (with resistance genes) was to be bred with the SM. The breeding process allows genes of both the parents (donor and SM) to be mixed. In the breeding process, the scientists did not want to lose the genes that gave special attributes to SM. The donor had to be selected carefully as the breeding process might bring in unwanted traits in the new variety. Therefore, selection of donor plant was the most crucial part.

Prior to this exercise, the scientists had heard about the work of Dr. Sukhwinder Singh from the Punjab Agricultural University (PAU). Under the Asian and National Rice Biotechnology Networks, supported by the Rockefeller Foundation and the Department of Biotechnology, in collaboration with the IRRI, Philippines, Dr. Singh had already created a rice variety called SS1113 with all the three genes *Xa21*, *xa13* and *xa5*. However, it was not very popular among farmers for cultivation. SS113 was created in the genetic background of PR106 and looked like a great donor. In a discussion that followed, the excitement of having all the three genes in PR106 background was soon consumed with a comment from Dr. A.P.K. Reddy. "Samba Mahsuri (SM) is like a beautiful vase. If we cross it with PR106, it will be broken into a thousand pieces. Our job will be to reassemble those pieces into the vase", he had opined. Finally, SS113 variety was chosen as the donor.

For the plan to succeed, two clear objectives needed to be achieved—retain the grain and cooking qualities of SM, and add the three resistance genes. Molecular Marker assisted Backcross Breeding program began towards developing an ISM variety that would be resistant to bacterial blight.

### **The three years of reassembling the 'vase'**

For Dr. Ramesh and his team, it took three years to reassemble the disease resistant SM variety, including all the three resistance genes. "We did a laborious background selection for enriching Samba Mahsuri genome component and selecting seeds that were triple heterozygous (having one copy each of *xa21*, *xa13* and *xa5*) for the three genes", recalls Dr. Ramesh. Finally, BC4F<sub>2</sub> genome was stabilized for three more generations BC4F<sub>5</sub>-F<sub>6</sub>. Dr. Ramesh comments with utmost confidence – "We never did any phenotypic selection. It was purely a molecular marker based selection". ISM was one of the first rice varieties to be developed in India through biotechnological interventions. The other was improved Pusa Basmati-1 in which bacterial blight resistance was introduced by the Indian Agricultural Research Institute (IARI) into the genetic background of Pusa Basmati-1, a semi-dwarf basmati variety that had been originally developed by Dr. Siddiqui.

The backcross-breeding program was laborious; scientists were busy, and three years passed very quickly. In 2002, BC4F<sub>2</sub> was obtained after rigorous selection. BC4F<sub>1</sub> had all the three genes added to the SM genetic background. It took another three years for stabilization of the variety and product development, which required breeding the ISM variety for a few more generations and monitoring the resistance.

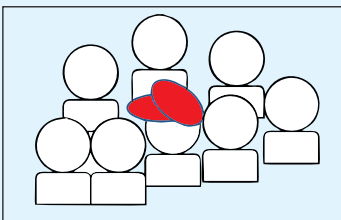


### The making of improved Samba Mahsuri

Ss1113 was crossed with Samba mahsuri (SM). The first generation plants (offspring of the cross) from these parents (SS1113 and SM) were backcrossed to SM to generate BC1F<sub>1</sub> plants. A backcross involves crossing the first generation to one of the parents. The BC1F<sub>1</sub> plants (segregating breeding plants) were evaluated using molecular markers for the presence of desired resistance genes and to identify those that had the maximum genomic contribution from the SM genome. This would help in recovery of the grain and cooking qualities of SM. The BC1F<sub>1</sub> plant, which was confirmed to have the desired molecular make up, was selected and backcrossed to SM. A total of four backcrosses were made with the recurrent parent, in this case SM. After each cross breeding cycle, the presence of three bacterial blight resistance genes using molecular methods was confirmed. The fourth generation of segregating population BC4F<sub>1</sub> (Back Cross 4 F<sub>1</sub>) had a genetic background that was close to 96% of the Samba Mahsuri genome. These BC4F<sub>1</sub> plants were selfed (both the parents now were from the BC4F<sub>1</sub> generation) and BC4F<sub>2</sub> was obtained. The desired outcome was to have Samba Mahsuri genome added with the three genes Xa21, xa13 and xa5.

BC: Backcross (1, 2, 3, 4 denotes the number of generations for which the backcross was performed)

### What is a molecular marker?



A molecular marker is a tag (DNA sequence) located close to a gene and always stays with the gene. In simple words if the presence of the tag is confirmed in a given sample, the gene is also present mandatorily. An analogy would be - If you have to spot out a single person in a crowd, it would be very difficult to do so.

However, if you provide a unique tag to this person, say a colorful headgear or a cap, he or she could be traced easily in the crowd. One does not have to look for the person but simply the headgear or hat. This is what a molecular marker does; it simply helps detect the presence of the desired gene or trait of interest.

## The final ordeal: Triumph over *Xanthomonas*

The success at molecular level was achieved, but the final confirmatory test was still pending. The litmus test was to infect the new variety, Improved Samba Mahsuri (ISM) directly with the pathogen, *Xanthomonas*. ISM was inoculated with the lethal organism. Infection experiments were conducted on both SM and ISM plants. The waiting period post inoculation was difficult to pass for the scientists. *Xanthomonas* had always been an undisputed winner in the battlefield of SM; however, this time it was fighting three new soldiers— *Xa21*, *xa13* and *xa5*.

Every day, the scientists inspected the infected plants with a bated breath. The first day, when the symptoms of leaf blight appeared on SM, the scientists inspected the ISM plants a number of times. There was no bad news for ISM, but the scientists chose to wait. Soon enough, while the leaves of SM plants started drying to death, the leaves of ISM stood green, erect and healthy. With this final ordeal passed, the scientists at CCMB and DRR/IIRR celebrated together. Finally, they had successfully deployed the three soldiers to counter *Xanthomonas* and Samba Mahsuri was now free from the shackles of the deadly pathogen.

Partner scientists at IIRR/DRR, under a program supported by the Department of Biotechnology, conducted station trials for yield and quality tests. Finally, the variety was tested in national field trials of ICAR throughout India under the AICRIP program. The variety was successful in field trials - exhibiting resistance to bacterial blight while also retaining the unique qualities of SM. In addition, a 20% yield increase was also recorded for ISM under the conditions of bacterial blight infestation.

Now, what was the new variety going to be called? "After the trials, it was decided mutually by CCMB and IIRR that the original name of the variety should be retained. Samba Mahsuri was very popular in the region and we thought a new name might interfere with the dissipation and popularization of the new variety. Also Samba Mahsuri

*The team of CCMB and IIRR scientists in a field of Improved Samba Mahsuri awaiting harvest near Kodad, in Nalgonda district, Telangana.*

*(Photo Courtesy: Dr. Ramesh V. Sonti, CCMB)*



was originally developed and named by ANGRAU, so we decided not to change the maiden name. ANGRAU was gracious in allowing us to keep the maiden name for the variety. Everyone was happy with the name- Improved Samba Mahsuri (ISM)", says Dr. Ramesh talking about the discussions the scientists had on the nomenclature.

## Commercializing ISM: Laboratory to fields

ISM was notified as a bacterial blight resistant variety in the Gazette of India in the year 2008 and released for commercial cultivation. It is now an officially registered variety under the Protection of Plant Varieties & Farmer's Rights Authority (PPV & FRA). CCMB and DRR/IIRR are the proud parents of this prodigy. To add jewels to the ISM's crown, CCMB and DRR/IIRR have been jointly awarded the CSIRs Award for S&T innovations for rural development 2015 and is the Biotech Product & Process Development and Commercialization Award for 2016 that was awarded by the Department of Biotechnology.

ISM is an excellent example of how science and technology have changed societies. For ISM to change the agrarian fate of the rice producing regions of India, the seeds had to reach the farmers. CCMB and DRR had also undertaken the task of ISM seed multiplication. ISM seeds were distributed to about 6,500 farmers under a CCMB- IIRR/DRR joint program called 'Blight Out' and was funded by the Council for Scientific and Industrial Research (CSIR).

In 2011, CCMB and IIRR entered into a Memorandum of Association (MoA) with private seed companies for large-scale production of ISM. Dr. Ramesh Sonti was invited for a lecture on ISM at the University of Hyderabad. Sitting in the audience were a few representatives from Sri Biotech, a microbiology company based in Hyderabad. After hearing the lecture, Sri Biotech expressed its interest in being the seed supplier for ISM. A license under a MoU with CCMB and DRR/IIRR was given to Sri Biotech for ISM seed multiplication. The first batch of seeds from Sri Biotech was distributed to farmers in Kurnool District of Andhra Pradesh. Kurnool's SM is considered the best and fetches the top prices in the market. Further, the area is a real hotspot for bacterial blight infections. About 20,000 hectares in Kurnool district was sown with ISM seeds.

While Sri Biotech took the leap in ISM seed production and was multiplying the seeds ably, an unfortunate event ended up in the exit of Sri Biotech after two years. One of the farmers complained that the resistance to bacterial blight had been broken down in his field. This was the last thing that the scientists wanted to hear for the variety, after years of hard work. It was a sporadic case, but imposed a question on the technology adopted to develop ISM. The scientists were shaken, but they postulated that the field might have grown a mixed batch of seeds contaminated with SM seeds. They took the samples from the field and tested it to

discover that the batch had mixing of the susceptible SM. The company, Sri Biotech, took the decision that it would focus on its core business of plant growth promoting microbiologicals and exited the seed business.

### Spreading the word on ISM

One of the farmers from Kurnool, Brahma Reddy, had obtained the seeds from the scientists in the year 2009. Reddy was a veteran Samba Mahsuri grower, growing the crop for fifteen years and had struggled with bacterial blight during several crop seasons. In 2009, his yield of SM had gone down to as low as 15 bags per acre due to the devastating *Xanthomonas* infection. In 2009, Reddy grew ISM on his field and SM on his father's fields. When the infection struck, Reddy's field was protected, while his father's was infected with blight disease. Now, not only his father, but also fellow farmers could also see the advantage of the new variety. Reddy ended up with almost 40 bags of rice from his field that were sown with ISM seeds. He had got such a wonderful harvest after many years!

"Brahma has now turned into a small businessman, following the success of ISM on his small field. He now multiplies and sells ISM seeds to other farmers. In his region, Brahma is now the brand ambassador for ISM popularization", chuckles Dr. Ramesh.



*Mr. Brahma Reddy with farmers to whom he supplied Improved Samba Mahsuri rice variety. Near Nandhyal, Kurnool district, Andhra Pradesh. (Photo Courtesy: Dr. Ramesh V. Sonti, CCMB)*



*Mr. Brahma Reddy with Dr. Ramesh in a rice field infected with bacterial leaf streak disease near Nandhyal, Andhra Pradesh.*

*(Photo Courtesy: Dr. Ramesh V. Sonti, CCMB)*

Farmers meetings were another strategy that was used for ISM popularization. Initially, the meetings represented farmers from the adjoining areas of Telengana and Andhra Pradesh, but later extended to Tamil Nadu. These meetings presented a different level of discourse for the scientists who now heard the real-life field experiences by the farmers.

It was a confluence of technological conversations and emotional narratives. The seed distribution drive at the farmers meetings kicked off successfully and the area under ISM cultivation was increased. Under the CSIR 800 scheme, seeds were multiplied, tested and treated with fungicides before being packed in the 10 kg bags that were distributed to farmers. ISM is now grown on about 130,000 hectares in Andhra Pradesh, Tamil Nadu, Telangana, Karnataka, Chhattisgarh and Bihar—geographical hotspots of the disease. The total estimated turnover for farmers growing ISM is about 1,250 crore INR. For their efforts on ISM popularization, CCMB and DRR were jointly adorned with CSIR Award for S&T Innovations for Rural Development – 2013. The award included a cash prize of 10 lakh rupees, a citation and a shield.

The efforts for popularization of ISM were captured by the press, and MetaHelix Life Sciences from Bengaluru approached CCMB and IIRR for technology license. The company, after signing a MoU with IIRR-CCMB in 2015, is now multiplying and selling ISM seeds. National Seeds corporation (NSC) outlets are also selling ISM seeds in the State of Bihar. The word has spread and farmers are now demanding new seed every year with a seed replacement rate of 70-80%.



According to the recent interim report from the National Institute of Agriculture Extension Management (MANAGE), it is estimated that ISM has been cultivated in an area of 130,000 hectares in seven states. The total value of the produce is estimated to be around 1250 crores INR (as per 2016 prices) and the trait value—the extra income that farmers are reported to have received from cultivation of ISM instead of SM—is close to 250 crores INR.

### **Gearing up for the future -- What if the resistance to bacterial blight breaks?**

When the scientists at CCMB-IIRR were breathing easy after their triumph against the toughest enemy, a moment of introspection arrived during a meeting in 2007 with Dr. Deo Mishra, a plant pathologist from Bayer Crop Sciences, Hyderabad. Dr. Mishra presented evidences supporting the fact that the volume of information available for variations/strains of *Xanthomonas* in India was inadequate, and that Bayer had a collection of more recent isolates of the pathogen. Alarmed, the scientists checked if these isolates could break down the three genes in ISM, and to their joy, discovered that none could break all the three.

However, there were isolates that could break down one or two of the three resistance genes. This was a confirmation of an observation that was originally made by Dr. R. Sridhar at the Central Rice Research Institute in Cuttack. It was found that a few of the isolates from North Eastern India could break *xa13* and *xa5* separately, but not when these were together. Here again the scientists found that presence of *xa5* was instrumental in maintaining the resistance capacity of the other two genes.

Now, CCMB, IIRR and Bayer Crop Sciences have pooled maximum pathogenic strains and have collaborated with CSIR-IMTECH, Chandigarh, which has undertaken next generation sequencing (NGS) based characterization. This has provided important insights into the nature of the variability of the bacterial blight pathogen in India. In collaboration with scientists at the University of California, Davis, our scientists have elucidated the genetic changes that are present in Indian strains of the pathogen that can break down the *Xa21* mediated resistance.

But what if the bacteria can indeed develop resistance and end up breaking down each of the individual genes, *Xa21*, *xa13* and *xa5*? To address this, researchers at IIRR and Punjab Agricultural University have discovered other novel resistance genes from wild rice species and have placed these genes in popularly cultivated rice varieties. An alternative method is to mutagenize SM and look for mutants, which confer good resistance against bacterial blight. Treating with chemical agents such as ethyl methane sulphonate can mutate SM seeds by introducing changes to the DNA. Finding out the mutated genes and screening for new DNA



markers for resistance genes will help us prepare for the future as the pathogens are always changing and evolving.

Other than bacterial blight, diseases like sheath blight caused by a soil fungus, also pose a great threat for rice farmers in India. While there are no naturally occurring variations in rice that are resistant to sheath blight, scientists have treated SM with chemicals, in a process called mutagenesis, to screen or discover changes in the DNA that can lead to resistance against the disease. Studies on developing tolerance against the rice insect Yellow stem borer are also underway. Further, certain rice variants generated via chemical mutagenesis have also exhibited traits such as longer grain size and higher yield, which may confer commercial appreciation. However, screening mutations after chemical treatment is a mammoth task. As it is a random process, one has to screen thousands of plants for several generations to score for resistance or tolerance traits. But the promise for this laborious work is huge.

### CSIR-800 Initiative

CSIR-800 is an initiative by CSIR aimed at bringing desired scientific and technological interventions in the areas of health, agriculture, and energy for improving the quality of life of the poor in India. It is catered to provide livelihood opportunities to an estimated 800 million people who fall under the rural poor or urban poor category.

When *Xanthomonas* raised its monstrous head after the famous cyclone Hudhud in 2014, and ate up majority of the fields growing SM in Andhra Pradesh, CSIR-800 initiative came to the rescue. “For Kharif 2014, we had distributed seeds of ISM to several farmers in East Godavari district under the CSIR 800 initiative”, says Dr. Ramesh. Now, the challenge that the agriculture departments are facing is to provide sufficient seeds of ISM to the farmers. This demand has created unscrupulous suppliers who are selling impure seeds of ISM. A report from MANAGE has flagged this issue, and has noted that seeds supplied by farmers, like Brahma Reddy, are of high quality. A proper institutional supplier of seeds, such as a reputed seed company, would also go a long way towards meeting the needs of the farmers.

#### CSIR 800 INITIATIVES FOR ISM

Dr. Mohan Rao, the Director of CCMB indicates that they decided to multiply and distribute ISM seeds in collaboration with DRR/IIRR. The multiplication and distribution

of Improved Samba Mahsuri for popularization was funded under the CSIR 800 scheme. Under this program 10 kg seed bags of ISM were distributed free of cost to many farming households in Telangana, Andhra Pradesh, Karnataka, Tamil Nadu, Chhattisgarh and Uttar Pradesh.

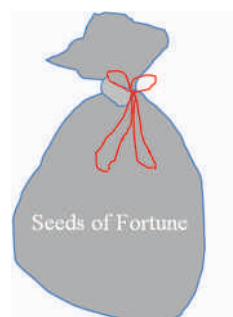
This was done in collaboration with Krishi Vigyan Kendras (KVKs), State Agriculture Departments and Agriculture Universities as well as progressive farmers who joined as partners.



*Team from CCMB and IIRR inspecting harvest of Improved Samba Mahsuri being dried in the courtyard of a farmer near Kodad Nalgonda district, Telangana. (Photo Courtesy: Dr. Ramesh Sonti, CCMB)*

Sitaramaiyah suddenly woke up. He had the best of sleep after many months. He saw Venkat approaching and waited for him while lying in his cot. “Do you want to come to the farmers meeting?” asked Venkat. Sitaramaiyah nodded his head in agreement; he was looking forward to finding answers to his questions at the farmers meeting.

“Nature holds all the forms of life that we see around us with a fine balance of interdependence. If *Xanthomonas* was a curse for the rice crop, the same crop also had the gift of *Xa21*, *xa 13* and *xa5* genes. Scientists have the training, creativity and patience to investigate the nature and its intricacies. There cannot be a solution without



identifying a problem. All it takes for a scientist to solve a problem is an idea. This time, the idea was to make intelligent use of three genes naturally available in the rice itself and solve the problem of bacterial blight”, Sitaramaiyah heard a scientist say as he stood spell bound. His heart was filled with tranquillity.

In the cool breeze, Sitaramaiyah walked home smelling his healthy, ripened crop. He had rediscovered his power to grow life on his fields; his hands could feel enormous strength. His greatest enemy was destroyed. His hands reached out for a sickle—it was time to harvest!

**Note:** *While Sitaramaiyah is a fictional character, he represents large number of farmers who have benefited from "Improved Samba Mahsuri"*

## Acknowledgements

The author acknowledges Dr. Ramesh V. Sonti, CCMB for his help, support and time.

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# SAMBHA MAHSURI'S ADVERSARY– *Xanthomonas oryzae*



## Let's Meet XOO

1

Xanthomonas are bacteria, which belong to a group of 27-30 species all of which cause diseases in plants.



*Xanthomonas oryzae* pv. *oryzae* or Xoo is rod shaped, non spore forming, and gram negative bacterium.



2

Xoo infects the rice plant and causes the bacterial blight disease. Bacterial Blight was first reported in 1884 in Japan.

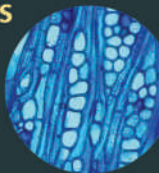


Symptoms include wilting of seedlings and leaves. The leaves acquire a yellowish color.



3

Initially, Xoo enters the plant through the hydathodes in leaf tip and leaf margin and finally the systemic infection occurs via Xylem, a tissue which carries water and minerals through the plants.



Xoo spreads through weeds and stubbles of already infected rice plants.

4

Xoo loves irrigated and low rainfed areas and strong winds as it spreads through ooze droplets present on the lesions of infected plants, akin to how flu virus spreads.



Xoo chooses tropical and temperate areas as its favorite travel destinations for spreading infections.



It loves warmth and feels strong at temperatures ranging between 25-34°C. Xoo is happy to sweat and loves humid environment with humidity as high as 60-70%.

The more nitrogen in the soil, the merrier Xanthomonas feels.



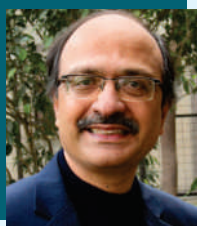


## About the Authors

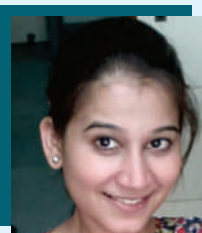


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**Nissy Nevil** is an optical physicist with interests in science policy. She graduated with a PhD in Physics from University of Antwerp, Belgium. Following her PhD, Nissy has taught science alongside exploring different career options that would allow her to apply her scientific skills to a broader domain. As part of this, she attended a workshop on Science and Technology (S & T) Policy organised by IISER Pune in March 2016. She has worked as S & T Policy intern with IISER Pune and later as a Management and Policy Consultant with IndiaBioscience based at NCBS, Bangalore.











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